1. General Information

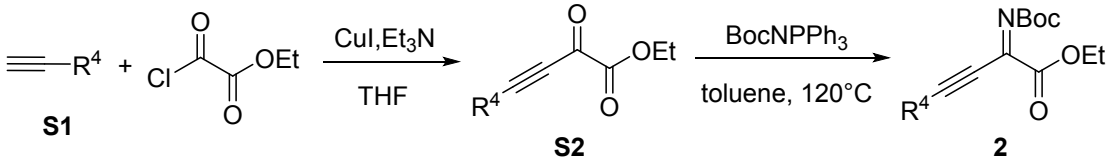
Chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. Chiral phosphoric acids **CPA1-CPA10** and racemic phosphoric acid were purchased from commercial suppliers. Solvents were dried and purified according to the standard procedures before use. Reactions were monitored by TLC. Racemic products were obtained from corresponding substrates catalyzed by racemic phophoric acid at room temperature. Flash column chromatography was performed on silica gels (200-300 mesh). ^{1}HNMR and ^{13}C NMR (300 or 400 and 75 or 100 MHz, respectively) spectra were recorded on a Bruker 300 or 400 MHz NMR spectrometer in $CDCl_3$ or DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm, DMSO-d_6,δ 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonances as the internal standard ($CDCl_3$, δ 77.16 ppm, DMSO-d_6, δ 39.52 ppm). All enantiomeric ratios were controlled by co-injections of the pure sample with the racemates. HRMS data were obtained on a Bruker Daltonics. Inc. mass instrument (ESI). Chiralpak IC-H, OD-H, AD-H, AY-H column was purchased from Daicel Chemical Industries (Hong Kong, China). Optical rotations were measured on a Perkin-Elmer 241 Polarimeter. Melting points were recorded on a Buchi Melting Point B-545.

2. Procedures and characterizations data of compounds

2.1 General produce of 5-aminoisoxazoles 1a-r

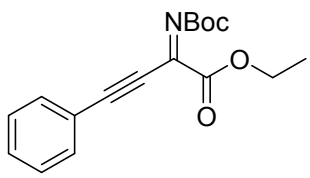
5-Aminoisoxazoles **1a-1r** were synthesized according to the procedures reported by our group.[1,2]

2.2 Synthesis of β,γ-alkynyl-α-imino esters 2a-n



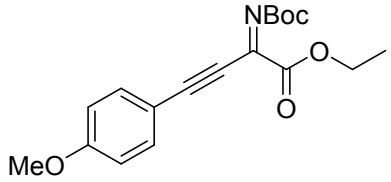
β,γ-Alkynyl-α-imino esters **2** were prepared based on the reported procedures.[3]

A two necked flask was charged with CuI (10 mol%) and THF (0.4 M), trimethylamine (2.0 equiv), alkyne **S1** (1.0 equiv) and ethyl 2-chloro-2-oxoacetate (1.2 equiv.) were added sequentially and the resulting mixture was stirred at room temperature for 2 days. The reaction was quenched by saturated aqueous $NaHCO_3$ solution and the aqueous phase was extracted with ethyl acetate. The organic phases were combined, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate 20:1) to give the product **S2**. Afterwards, an oven-dried round bottom was added ketoesters **S2** (1.0 equiv), N-Boc-triphenyliminophosphorane (1.2 equiv.) and toluene. The mixture was heated to 120°C and stirred for 24h. After cooling to room temperature, the mixture was concentrated under vacuum. The residue was purified by silica gel chromatography (petroleum ether/ ethyl acetate 20:1) to give the product **2**.



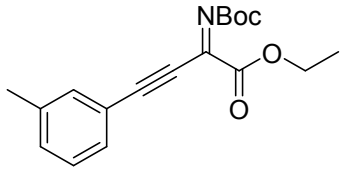
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-phenylbut-3-ynoate (2a): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (dt, *J* = 7.0, 1.5 Hz, 2H), 7.51-7.43 (m, 1H), 7.43-7.34 (m, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.58 (s, 9H), 1.41 (t, *J* = 7.1 Hz,

3H).



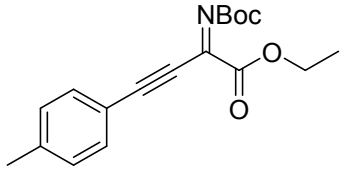
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-methoxyphenyl)but-3-ynoate (2b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 4.41 (q, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 1.58 (s, 9H), 1.40 (t, *J* = 7.1 Hz, 3H).

Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(*m*-tolyl)but-3-ynoate (2c)



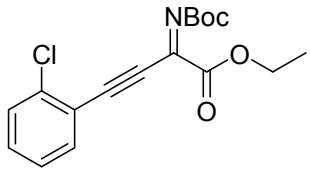
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.6 Hz, 2H), 7.28 (s, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.58 (s, 9H), 1.41 (t, *J* = 7.1 Hz, 3H).

Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(*p*-tolyl)but-3-ynoate (2d)



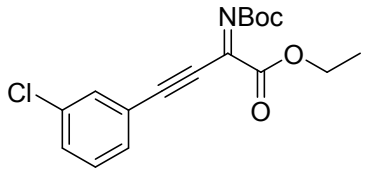
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.57 (s, 9H), 1.40 (d, *J* = 7.2 Hz, 3H).

Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(2-chlorophenyl)but-3-ynoate (2e)



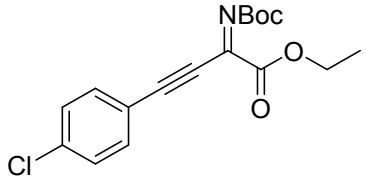
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.43-7.35 (m, 1H), 7.30 (dd, *J* = 7.5, 1.5 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.57 (s, 9H), 1.41 (t, *J* = 7.2 Hz, 3H).

Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(3-chlorophenyl)but-3-ynoate (2f)



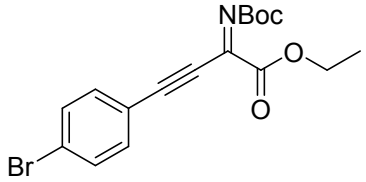
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.49 – 7.38 (m, 2H), 7.33 (t, *J* = 7.9 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.58 (s, 9H), 1.41 (t, *J* = 7.8 Hz, 3H).

Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-chlorophenyl)but-3-ynoate (2g)



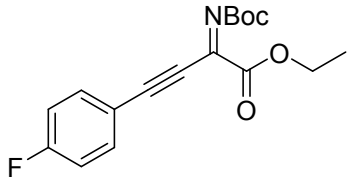
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.7 Hz, 2H), 4.42 (q, *J* = 7.2 Hz, 2H), 1.57 (s, 9H), 1.41 (t, *J* = 7.2 Hz, 3H).

Ethyl (*E*)-4-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)imino)but-3-ynoate (2h)

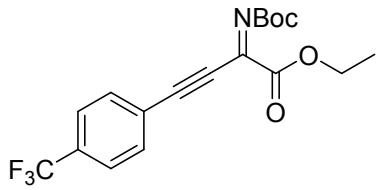


^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.57 (s, 9H), 1.41 (t, *J* = 7.3 Hz, 3H).

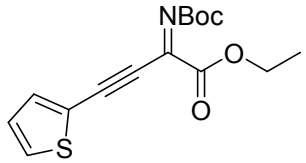
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-fluorophenyl)but-3-ynoate (2i)



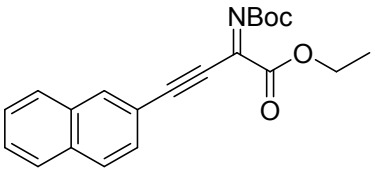
^{1}H NMR (300 MHz, CDCl3) δ 7.61–7.49 (m, 2H), 7.15–7.03 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.57 (s, 9H), 1.41 (t, *J* = 7.1 Hz, 3H).



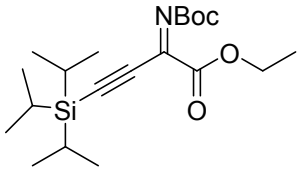
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-(trifluoromethyl)phenyl)but-3-ynoate (2j): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (s, 4H), 4.43 (q, *J* = 6.9 Hz, 2H), 1.57 (s, 9H), 1.42 (t, *J* = 7.1 Hz, 3H).



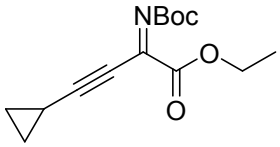
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(thiophen-2-yl)but-3-ynoate (2k): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 5.0 Hz, 1H), 7.46 (d, *J* = 3.8 Hz, 1H), 7.08 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.42 (q, *J* = 7.0 Hz, 2H), 1.59 (s, 9H), 1.41 (t, *J* = 7.2 Hz, 3H).



Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(naphthalen-2-yl)but-3-ynoate (2l): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.85 (dd, *J* = 8.8, 2.9 Hz, 3H), 7.69–7.45 (m, 3H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.61 (s, 9H), 1.43 (t, *J* = 7.1 Hz, 3H).

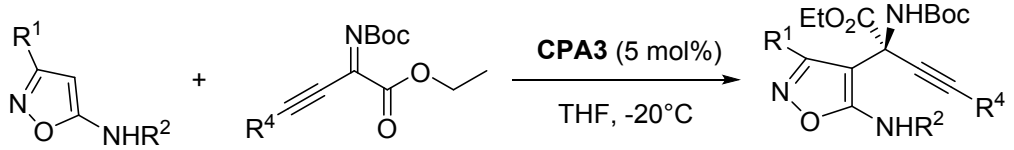


Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(triisopropylsilyl)but-3-ynoate (2m): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.36 (q, *J* = 7.2 Hz, 2H), 1.54 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.10 (d, *J* = 3.9 Hz, 21H).

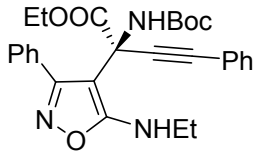


Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-cyclopropylbut-3-ynoate (2n): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.35 (q, *J* = 7.1 Hz, 2H), 1.54 (s, 9H), 1.47 (dt, *J* = 8.3, 5.0 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.01 (dt, *J* = 8.5, 2.9 Hz, 2H), 0.95 – 0.90 (m, 2H).

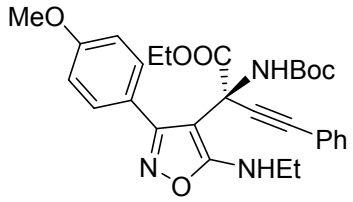
2.3 Catalytic enantioselective Mannich reaction of 5-amino-isoxazole 1 with β,γ-alkynyl-α-imino ester 2:



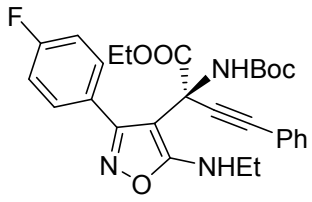
5-Amino-isoxazole **1** (0.10 mmol), β,γ-alkynyl-α-imino ester **2** (0.12 mmol) and **CPA3** (2.9 mg, 5 mol%) were dissolved in THF (0.5 mL, 0.2 M) in a flame-dried vial equipped with a magnetic stirring bar. The reaction mixture was stirred at -20 °C for 36 hours. The mixture was subjected to chromatography on silica gel (petroleum ether/ EtOAc =10:1) to afford the desired product **3**.



Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3aa): white solid, m.p.: 125.1-126.6 °C, 48.5 mg, 99% yield, ee = 95%, HPL C conditions: Chiralpak IC-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 6.512 min., t_{minor} = 6.965 min.). $[\alpha]_D^{20}$ = -84.5 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.45 (m, 2H), 7.42-7.29 (m, 8H), 6.18 (s, 2H), 3.91 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.58-3.44 (m, 3H), 1.46 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.36, 168.13, 162.49, 154.18, 131.70, 129.81, 129.26, 129.16, 128.77, 128.24, 128.04, 121.83, 87.22, 84.75, 84.63, 80.39, 63.26, 53.38, 37.90, 28.32, 15.59, 13.47. HRMS (ESI) Calcd for $C_{28}H_{32}N_3O_5^+$ $[M+H]^+$ 490.2337; Found: 490.2336.

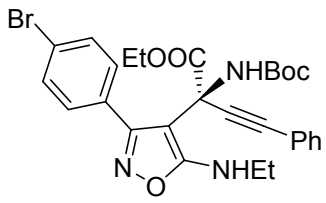


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl)isoxazol-4-yl)-4-phenylbut-3-ynoate (3ba): white solid, m.p.: 127.7-128.3 °C, 58.7 mg, 98% yield, ee = 94%, HPLC conditions: ChiralpakAD-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.874 min., t_{minor} = 7.161 min.). $[\alpha]_D^{20}$ = -81.0 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.39 (m, 2H), 7.32 (q, *J* = 5.9, 5.2 Hz, 5H), 6.95-6.84 (m, 2H), 6.15 (s, 2H), 3.94 (q, *J* = 8.7, 7.3 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 1H), 3.54-3.45 (m, 2H), 1.46 (s, 9H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.24, 162.25, 160.39, 154.19, 131.69, 130.48, 128.76, 128.24, 121.99, 121.86, 113.48, 87.20, 84.80, 84.60, 80.39, 63.31, 55.20, 53.40, 37.86, 28.31, 15.60, 13.52. HRMS (ESI) Calcd. for $C_{29}H_{34}N_3O_6^+$ $[M+H]^+$ 520.2442; Found: 520.2391.

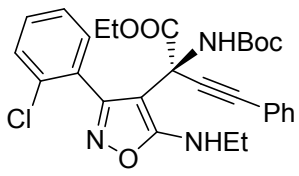


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethyl-amino)-3-(4-fluorophenyl)isoxazol-4-yl)-4-phenylbut-3-ynoate (3ca): white solid, m.p.:110.2-111.0 °C, 48.8 mg,

96% yield, ee = 92%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.777 min., t_{minor} = 5.823 min.). $[\alpha]_D^{20}$ = -89.0 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.41 (m, 2H), 7.40-7.25 (m, 5H), 7.07 (dd, *J* = 9.9, 7.4 Hz, 2H), 6.15 (s, 2H), 3.97 (t, *J* = 9.0 Hz, 1H), 3.62 (s, 1H), 3.55-3.46 (m, 2H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.31, 168.12, 163.37 (d, *J* = 247.43 Hz), 161.63, 154.16, 131.64, 131.11 (d, *J* = 8.33 Hz), 128.86, 128.28, 125.87 (d, *J* = 3.08 Hz), 121.70, 115.11 (d, *J* = 21.53 Hz), 87.06, 84.84, 84.61, 80.54, 64.90, 63.34, 53.41, 37.88, 28.29, 15.57, 13.52. HRMS (ESI) Calcd. for $C_{28}H_{31}FN_3O_5^+$ $[M+H]^+$ 508.2242; Found: 508.2234.

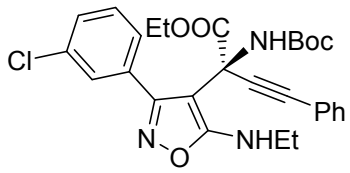


Ethyl (*S*)-2-(3-(4-bromophenyl)-5-(ethylamino)isoxazol-4-yl)-2-((*tert*-butoxycarbonyl)amino)-4-phenylbut-3-ynoate (3da): white solid, m.p.:126.1–128.5 °C, 56.2 mg, 99% yield, ee = 88%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.410 min., t_{minor} = 6.499 min.). $[\alpha]_D^{20}$ = -73.3 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 5H), 6.12 (s, 2H), 4.07 – 3.92 (m, 1H), 3.68 (s, 1H), 3.58-3.41 (m, 2H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.25, 168.09, 161.62, 154.15, 131.62, 131.22, 130.81, 128.85, 128.28, 123.69, 121.64, 86.88, 85.02, 84.58, 80.60, 63.39, 53.49, 37.89, 28.27, 15.57, 13.56. HRMS (ESI) Calcd for $C_{28}H_{31}BrN_3O_5^+$ $[M+H]^+$ 568.1442; Found: 568.1430.

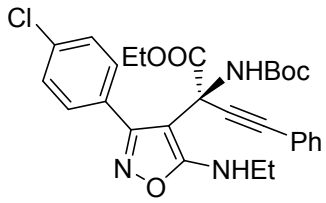


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(2-chlorophenyl)-5-(ethylamino)isoxazol-4-yl)-4-phenylbut-3-ynoate (3ea): yellow solid, m.p.:100.6-102.8 °C, 51.9 mg, 99% yield, ee = 84%, HPLC conditions: Chiralpak IC-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 18.661 min., t_{minor} = 9.796 min.). $[\alpha]_D^{20}$ = -42.4 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ

7.38-7.21 (m, 9H), 6.11 (s, 1H), 5.80 (s, 1H), 4.09 (d, *J* = 8.8 Hz, 1H), 3.93 (s, 1H), 3.51 (qd, *J* = 7.2, 5.8 Hz, 2H), 1.42 (s, 9H), 1.27 (dq, *J* = 13.9, 7.2, 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.80, 167.63, 159.86, 153.85, 134.19, 131.88, 131.63, 130.36, 129.34, 128.96, 128.69, 128.10, 126.06, 121.73, 87.26, 84.78, 84.52, 80.36, 63.13, 53.65, 37.85, 28.23, 15.50, 13.65. HRMS (ESI) Calcd. for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1939.

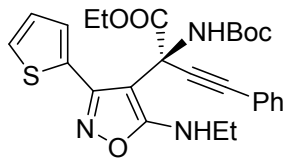


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(3-chlorophenyl)-5-(ethylamino)isoxazol-4-yl)-4-phenylbut-3-ynoate (3fa): light yellow solid, m.p.: 101.5–104.0 °C, 50.8 mg, 97% yield, ee = 86%, HPLC condition: Chiralpak IC-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 7.125 min., t_{minor} = 9.113 min.). $[\alpha]_D^{20}$ = -61.2 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.46-7.26 (m, 8H), 6.10 (d, *J* = 20.2 Hz, 2H), 4.01 (dd, *J* = 10.6, 7.1 Hz, 1H), 3.71 (d, *J* = 6.9 Hz, 1H), 3.56-3.43 (m, 2H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.22, 167.99, 161.31, 154.11, 133.90, 131.62, 129.26, 128.83, 128.21, 127.41, 121.59, 86.99, 84.96, 84.52, 80.55, 63.40, 53.40, 37.86, 28.24, 15.52, 13.49. HRMS (ESI) Calcd. for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1927.

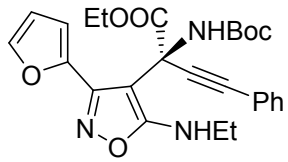


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(4-chlorophenyl)-5-(ethylamino)isoxazol-4-yl)-4-phenylbut-3-ynoate (3ga): yellow solid, m.p.: 134.1-135.9 °C, 51.9 mg, 99% yield, ee = 89%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.520 min., t_{minor} = 9.050 min.). $[\alpha]_D^{20}$ = -78.7 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.40 (m, 2H), 7.40-7.33 (m, 2H), 7.32-7.28 (m, 5H), 6.12 (s, 2H), 3.99 (dq, *J* = 13.8, 7.2 Hz, 1H), 3.65 (s, 1H), 3.56-3.44 (m, 2H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.28, 168.10, 161.58, 154.16, 135.42, 131.63, 130.55, 128.86, 128.28, 121.66, 86.95, 84.97, 84.59,

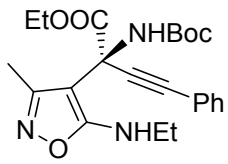
80.59, 63.38, 53.46, 37.90, 28.29, 15.57, 13.55. HRMS (ESI) Calcd. for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1936.



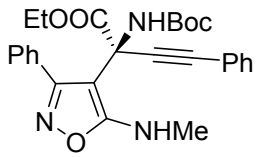
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(thiophen-2-yl)isoxazol-4-yl)-4- phenylbut-3-ynoate (3ha): white solid, m.p.: 110.7-111.4 °C, 49.1 mg, 99% yield, ee = 94%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 10/90, 1.0 mL/min., t_{major} = 7.192 min., t_{minor} = 9.381 min.). $[\alpha]_D^{20}$ = -52.2 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45-7.27 (m, 6H), 7.24 (d, *J* = 3.6 Hz, 1H), 7.06 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.29 (s, 1H), 6.10 (s, 1H), 4.00 (dq, *J* = 10.5, 7.1 Hz, 1H), 3.72 (s, 1H), 3.50 (qd, *J* = 7.2, 5.8 Hz, 2H), 1.45 (s, 9H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.64, 168.16, 156.59, 154.18, 131.72, 129.40, 129.24, 128.94, 128.35, 127.29, 127.19, 121.66, 87.27, 84.70, 80.42, 63.54, 53.26, 37.90, 28.32, 15.54, 13.46. HRMS (ESI) Calcd for $C_{26}H_{30}N_3O_5S^+$ $[M+H]^+$ 496.1901; Found: 496.1836.



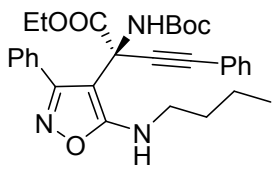
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(furan-2-yl)isoxazol-4-yl)-4-phenylbut-3-ynoate (3ia): yellow oil, 45.1 mg, 94% yield, ee = 92%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane:10/90, 1.0 mL/min., t_{major} = 7.853 min., t_{minor} = 11.927 min.). $[\alpha]_D^{20}$ = -76.2 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.47-7.39 (m, 2H), 7.37-7.28 (m, 3H), 6.81- 6.71 (m, 1H), 6.45 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.32 (s, 1H), 6.12 (s, 1H), 4.09 (dq, *J* = 10.3, 7.1 Hz, 1H), 3.96 (d, *J* = 8.3 Hz, 1H), 3.55-3.42 (m, 2H), 1.42 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.38, 154.06, 153.15, 144.14, 143.36, 131.74, 128.98, 128.37, 121.62, 111.33, 110.57, 87.10, 84.76, 80.16, 63.40, 53.28, 37.96, 28.29, 15.49, 13.48. HRMS (ESI) Calcd. for $C_{26}H_{30}N_3O_6^+$ $[M+H]^+$ 480.2129; Found: 480.2106.



Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-methylisoxazol-4-yl)-4-phenylbut-3-ynoate (3ja): yellow oil, 42.4 mg, 99% yield, ee = 89%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 6.079 min., t_{minor} = 8.919 min.). $[\alpha]_D^{20}$ = -20.8 (c 1.0,dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (dt, *J* = 7.9, 2.3 Hz, 2H), 7.35 (dd, *J* = 5.2, 2.4 Hz, 3H), 5.66 (d, *J* = 18.2 Hz, 2H), 4.44-4.09 (m, 2H), 3.38 (td, *J* = 7.3, 5.8 Hz, 2H), 2.22 (s, 3H), 1.44 (s, 9H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.40, 166.66, 158.77, 153.83, 131.60, 128.95, 128.45, 121.83, 85.99, 85.28, 84.85, 80.69, 63.27, 54.16, 37.78, 28.23, 15.58, 13.88, 11.70. HRMS (ESI) Calcd for $C_{23}H_{30}N_3O_5^+$ $[M+H]^+$ 428.2180; Found: 42.2159.

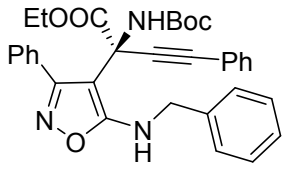


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(methylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3la): white solid, m.p.: 126.5-130.1 °C, 46.2 mg, 97% yield, ee = 93%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.623 min., t_{minor} = 5.757 min.). $[\alpha]_D^{20}$ = -95.7 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.42-7.36 (m, 3H), 7.31 (t, *J* = 3.2 Hz, 5H), 6.22 (s, 1H), 6.13 (s, 1H), 3.91 (d, *J* = 11.3 Hz, 1H), 3.50 (s, 1H), 3.13 (dd, *J* = 5.5, 2.1 Hz, 3H), 1.46 (s, 9H), 1.07 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.90, 168.12, 162.65, 154.26, 131.75, 129.74, 129.31, 129.14, 128.81, 128.26, 128.07, 121.79, 87.27, 84.60, 80.44, 63.32, 53.28, 29.62, 28.33, 13.46. HRMS(ESI) Calcd for$C_{27}H_{30}N_3O_5^+$ $[M+H]^+$ 476.2180; Found: 476.2164.

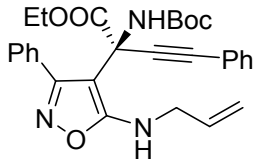


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(butylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3ma): white solid, m.p.: 92.7–94.6 °C, 51.3 mg, 99% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 10/90, 1.0 mL/min, t_{major} = 4.956 min., t_{minor} = 12.587 min.). $[\alpha]_D^{20}$ = -73.8 (c 1.0,

dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.45 (m, 2H), 7.45-7.35 (m, 3H), 7.31 (d, *J* = 2.7 Hz, 5H), 6.25 (s, 2H), 3.88 (d, *J* = 8.0 Hz, 1H), 3.46 (q, *J* = 6.7 Hz, 3H), 1.68-1.57 (m, 2H), 1.46 (s, 9H), 1.39 (t, *J* = 7.8 Hz, 2H), 1.07 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.42, 168.13, 162.49, 154.21, 131.69, 129.80, 129.25, 129.13, 128.75, 128.21, 128.03, 121.81, 86.97, 84.71, 84.55, 80.39, 63.25, 53.36, 42.66, 32.19, 28.29, 19.80, 13.62, 13.45. HRMS (ESI) Calcd for $C_{30}H_{36}N_3O_5^+$ $[M+H]^+$ 518.2649; Found: 518.2633.

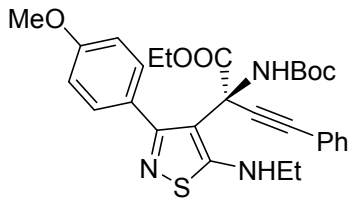


Ethyl (*S*)-2-(5-(benzylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl)amino)-4-phenylbut-3-ynoate (3na): light yellow solid, m.p.: 130.2-131.7 ^{o}C, 54.6 mg, 99% yield, ee = 93%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane :10/90, 1.0 mL/min., t_{major} = 7.380 min., t_{minor} = 12.349 min.). $[\alpha]_D^{20}$ = -73.9 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.48 (m, 2H), 7.44-7.39 (m, 5H), 7.31-7.18 (m, 8H), 6.70 (s, 1H), 6.31 (s, 1H), 4.78-4.60 (m, 2H), 3.89 (dq, *J* = 14.2, 7.3 Hz, 1H), 3.45 (s, 1H), 1.48 (s, 9H), 1.06 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.05, 162.58, 154.26, 138.53, 131.72, 129.68, 129.35, 129.10, 128.72, 128.47, 128.18, 128.10, 127.52, 127.23, 121.65, 87.71, 84.62, 84.52, 80.48, 63.33, 53.21, 46.94, 28.32, 13.43. HRMS (ESI) Calcd for $C_{33}H_{34}N_3O_5^+$ $[M+H]^+$ 552.2493; Found: 552.2474.

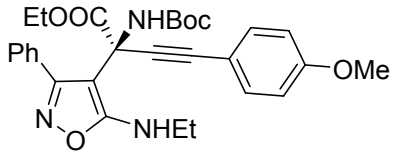


Ethyl (*S*)-2-(5-(allylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl)amino)-4-phenylbut-3-ynoate (3oa): yellow solid, m.p.: 126.4-128.3 ^{o}C, 49,7 mg, 99% yield, ee = 94%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.215 min., t_{minor} = 9.114 min.). $[\alpha]_D^{20}$ = -79.8 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.47 (m, 2H), 7.41-7.37 (m, 3H), 7.36-7.26 (m, 5H), 6.39 (s, 1H), 6.26 (s, 1H), 6.04 – 5.91 (m, 1H), 5.36 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.23-5.02 (m, 1H), 4.11 (ddt, *J* = 6.8, 5.3, 1.7 Hz, 2H), 3.89 (t, *J* = 9.0 Hz, 1H), 3.48 (s, 1H), 1.46 (s, 9H), 1.07 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.08, 162.60, 154.22,

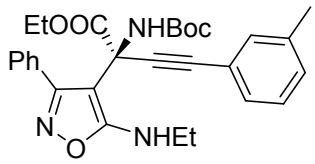
134.57, 131.77, 129.70, 129.32, 129.13, 128.80, 128.22, 128.08, 121.75, 116.08, 87.65, 84.62, 80.47, 63.32, 53.28, 45.32, 28.32, 13.45. HRMS (ESI) Calcd for $C_{29}H_{32}N_3O_5^+$ $[M+H]^+$ 502.2336; Found: 502.2321.



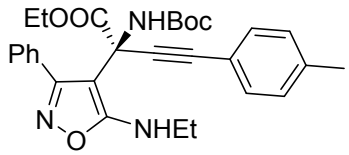
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl)isothiazol-4-yl)-4-phenylbut-3-ynoate (3qa): light yellow solid, m.p.: 156.3–158.2 °C, 37.5 mg, 70% yield, ee = 36% HPLC conditions: Chiralpak IC-H (isopropyl alcohol/n-hexane: 30/70, 1.0 mL/min., t_{major} = 21.231 min., t_{minor} = 28.674 min.). $[\alpha]_D^{20}$ = -75.8 (c 1.0, dichloromethane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.36 (m, 2H), 7.36-7.26 (m, 5H), 6.91-6.78 (m, 2H), 6.64 (s, 1H), 6.20 (s, 1H), 4.06-3.91 (m, 1H), 3.79 (s, 3H), 3.70 (d, *J* = 9.0 Hz, 1H), 3.23 (m, 2H), 1.46 (s, 9H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.30, 167.25, 159.91, 154.35, 131.69, 130.51, 129.79, 128.71, 128.24, 122.10, 113.12, 107.36, 85.44, 85.24, 63.27, 55.72, 55.22, 42.93, 28.38, 14.57, 13.55. HRMS (ESI) Calcd for $C_{29}H_{34}N_3O_5S^+$ $[M+H]^+$ 536.2214; Found: 536.2223.



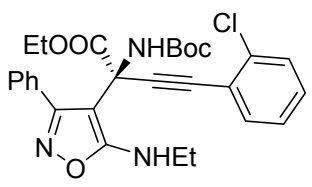
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-methoxyphenyl)but-3-ynoate (3ab): light yellow solid, m.p.: 109.2–110.5 °C, 51.5 mg, 99% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min, t_{major} = 5.469 min., t_{minor} = 16.006 min.). $[\alpha]_D^{20}$ = -75.2 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.44 (m, 2H), 7.39 (dt, *J* = 4.9, 3.0 Hz, 3H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.87-6.76 (m, 2H), 6.16 (s, 2H), 3.91 (dd, *J* = 10.6, 7.0 Hz, 1H), 3.80 (s, 3H), 3.61-3.42 (m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.27, 162.49, 159.97, 154.18, 133.19, 129.84, 129.24, 129.16, 128.04, 113.89, 113.83, 87.35, 84.69, 83.35, 80.31, 63.22, 55.26, 53.37, 37.90, 28.33, 15.61, 13.49. HRMS (ESI) Calcd for $C_{29}H_{34}N_3O_6^+$ $[M+H]^+$ 520.2442; Found: 520.2429.



Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(*m*-tolyl)but-3-ynoate (3ac): white solid, m.p.: 106.5–109.6 °C, 50.0 mg, 99% yield, ee = 84%, HPLC conditions: Chiralpak IC-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min, t_{major} = 6.399 min., t_{minor} = 7.249 min.). $[\alpha]_D^{20}$ = -86.4 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.46 (m, 2H), 7.44-7.32 (m, 3H), 7.16 (d, *J* = 4.1 Hz, 4H), 6.17 (s, 2H), 3.91 (dd, *J* = 10.5, 7.0 Hz, 1H), 3.64-3.42 (m, 3H), 2.31 (s, 3H), 1.46 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J*= 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.38, 169.17, 163.50, 155.17, 138.97, 133.33, 130.80, 130.67, 130.26, 130.16, 129.75, 129.14, 129.06, 122.61, 88.24, 85.82, 85.33, 81.37, 64.27, 54.32, 38.90, 29.32, 22.13, 16.59, 14.48. HRMS (ESI) Calcd for $C_{29}H_{34}N_3O_5^+$ $[M+H]^+$ 504.2493; Found: 504.2476.

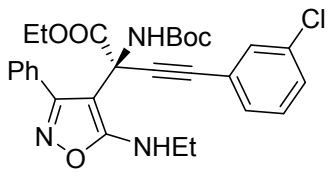


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(*p*-tolyl)but-3-ynoate (3ad): white solid, m.p.: 114.9-117.2 °C, 50.0 mg, 99% yield, ee = 89%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.778 min., t_{minor} = 11.191 min.). $[\alpha]_D^{20}$ = -98.5 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.44 (m, 2H), 7.39 (dt, *J* = 4.9, 3.0 Hz, 3H), 7.27 (d, *J* = 8.6 Hz, 2H), 6.87-6.76 (m, 2H), 6.16 (s, 2H), 3.91 (dd, *J* = 10.6, 7.0 Hz, 1H), 3.80 (s, 3H), 3.61-3.42 (m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.21, 162.48, 154.17, 139.02, 131.59, 129.81, 129.25, 129.14, 129.01, 128.04, 118.70, 86.68, 84.80, 84.00, 80.33, 63.24, 53.33, 37.89, 28.31, 21.46, 15.59, 13.46. HRMS (ESI) Calcd for $C_{29}H_{33}N_3O_5H^+$ $[M+H]^+$ 504.2493; Found: 504.2482.

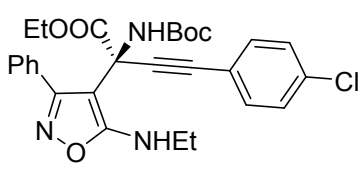


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(2-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl) but-3-ynoate (3ae): white solid, m.p.: 126.1-128.4 °C, 50.3

mg, 96% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.040 min., t_{minor} = 7.766 min.). $[\alpha]_D^{20}$ = -115.0 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.43 (m, 2H), 7.43-7.30 (m, 5H), 7.29-7.22 (m, 1H), 7.18 (td, *J* = 7.5, 1.4 Hz, 1H), 6.23 (d, *J* = 25.9 Hz, 2H), 3.93 (dq, *J* = 14.4, 7.3 Hz, 1H), 3.62-3.40 (m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.26, 167.90, 162.43, 154.01, 135.95, 133.48, 129.83, 129.73, 129.23, 129.19, 129.13, 128.02, 126.37, 121.81, 89.80, 86.78, 81.24, 80.38, 63.31, 53.42, 37.91, 28.27, 15.55, 13.48. HRMS (ESI) Calcd for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1932.

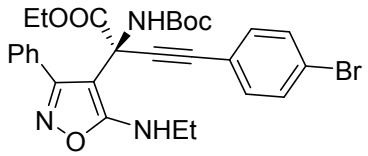


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(3-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl) but-3-ynoate (3af): light yellow solid, m.p.: 107.1-109.6 °C, 51.9 mg, 99% yield, ee = 89%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.097 min., t_{minor} = 5.100 min.). $[\alpha]_D^{20}$ = -78.3 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56-7.43 (m, 2H), 7.43-7.33 (m, 3H), 7.33-7.16 (m, 4H), 6.14 (s, 2H), 3.92 (t, *J* = 8.5 Hz, 1H), 3.65 -3.39 (m, 3H), 1.46 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.28, 167.91, 162.51, 154.23, 134.05, 131.61, 129.75, 129.70, 129.46, 129.32, 129.17, 129.03, 128.06, 123.50, 87.38, 85.97, 83.26, 80.60, 63.38, 53.39, 37.88, 28.28, 15.61, 13.50. HRMS (ESI) Calcd for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1935.

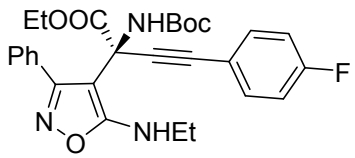


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ag): light yellow solid, m.p.: 110.8-112.7 °C, 51.9 mg, 99% yield, ee = 95%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.000 min., t_{minor} = 11.618 min.). $[\alpha]_D^{20}$ = -95.5 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53-7.44 (m, 2H), 7.44-7.33 (m, 3H), 7.30-7.19 (m, 4H), 6.14 (s, 2H), 3.92 (t, *J* = 8.9 Hz, 1H), 3.63-3.41

(m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.6 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.29, 167.96, 162.48, 154.22, 134.86, 132.90, 129.71, 129.29, 129.15, 128.59, 128.04, 120.27, 87.36, 85.69, 83.56, 80.53, 63.34, 53.39, 37.86, 28.27, 15.62, 13.49. HRMS (ESI) Calcd for $C_{28}H_{31}ClN_3O_5^+$ $[M+H]^+$ 524.1947; Found: 524.1930.

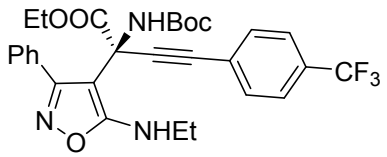


Ethyl (*S*)-4-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ah): white solid, m.p.: 62.8-66.8 °C, 56.2 mg, 99% yield, ee = 95%, HPLC conditions: Chiralpak OD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.205 min., t_{minor} = 11.986 min.). $[\alpha]_D^{20}$ = -86.7 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.45 (m, 2H), 7.45-7.33 (m, 5H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.14 (s, 2H), 3.90 (q, *J* = 8.3, 6.9 Hz, 1H), 3.62-3.42 (m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.25, 167.91, 162.46, 154.21, 133.08, 131.52, 129.73, 129.26, 129.16, 128.02, 123.10, 120.75, 86.97, 85.93, 83.65, 80.54, 63.31, 53.48, 37.86, 28.27, 15.60, 13.48. HRMS (ESI) Calcd for $C_{28}H_{31}BrN_3O_5^+$ $[M+H]^+$ 568.1442; Found: 568.1432.

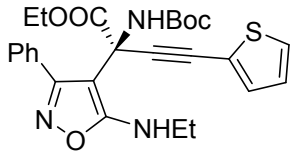


Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-fluorophenyl)but-3-ynoate (3ai): yellow solid, m.p.: 104.5-108.9 °C, 50.3 mg, 99% yield, ee = 94%, HPLC conditions: Chiralpak OD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.802 min., t_{minor} = 10.378 min.). $[\alpha]_D^{20}$ = -83.6 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52-7.45 (m, 2H), 7.41 – 7.34 (m, 3H), 7.30 (d, *J* = 9.3 Hz, 2H), 7.02-6.93 (m, 2H), 6.16 (s, 2H), 3.89 (d, *J* = 8.6 Hz, 1H), 3.58-3.43 (m, 3H), 1.45 (s, 9H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.31, 168.06, 162.72 (d, *J* = 248.93 Hz), 162.50, 154.22, 133.64 (d, *J* = 8.33 Hz), 129.74, 129.28, 129.15, 128.04, 117.87 (d, *J* = 3.45 Hz), 115.57 (d, *J* = 22.05 Hz), 87.11, 84.44, 83.63, 80.48, 63.31, 53.34, 37.87,

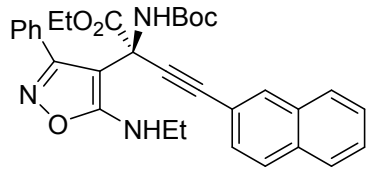
28.29, 15.61, 13.49. HRMS (ESI) Calcd for $C_{28}H_{31}FN_3O_5^+$ $[M+H]^+$ 508.2242; Found: 508.2219.



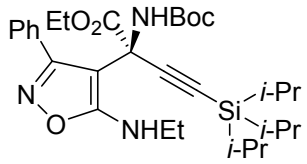
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-(trifluoro methyl)phenyl)but-3-ynoate (3aj): white solid, m.p.: 56.1-62.6 °C, 53.0 mg, 95% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min, t_{major} = 4.002 min, t_{minor} = 6.120 min). $[\alpha]_D^{20}$ = -84.0 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.52-7.45 (m, 2H), 7.39 (dd, *J* = 6.1, 2.7 Hz, 5H), 6.17 (s, 2H), 3.93 (s, 1H), 3.64 – 3.43 (m, 3H), 1.46 (s, 9H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.29, 167.86, 162.53, 154.29, 131.98, 130.53 (q, *J* = 32.63 Hz), 129.77, 129.33, 129.25, 128.08, 125.71, 125.18 (q, *J* = 3.83 Hz), 123.76 (q, *J* = 270.60 Hz), 87.32, 86.89, 83.34, 80.71, 63.42, 53.59, 37.92, 28.31, 15.64, 13.52. HRMS (ESI) Calcd for $C_{29}H_{31}F_3N_3O_5^+$ $[M+H]^+$ 558.2210; Found: 558.2177.



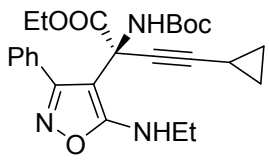
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(thiophen-2-yl)but-3-ynoate (3ak): yellow solid, m.p.: 101.9-104.8 °C, 48.5 mg, 97% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.692 min., t_{minor} = 8.681 min.). $[\alpha]_D^{20}$ = -92.7 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54-7.44 (m, 2H), 7.39 (q, *J* = 3.5 Hz, 3H), 7.26 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.11 (d, *J* = 3.6 Hz, 1H), 6.95 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.14 (s, 2H), 3.90 (d, *J* = 9.5 Hz, 1H), 3.60-3.44 (m, 3H), 1.45 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.29, 167.89, 162.46, 154.17, 132.62, 129.72, 129.30, 129.16, 128.05, 127.76, 126.92, 121.64, 88.52, 86.99, 80.55, 78.19, 63.36, 53.63, 37.92, 28.30, 15.60, 13.47. HRMS (ESI) Calcd. for $C_{26}H_{29}N_3O_5SH^+$ $[M+H]^+$ 496.1901; Found: 496.1889.



Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(naphthalen-2-yl)but-3-ynoate (3al): yellow solid, m.p.: 115.9-118.2 °C, 53.5 mg, 99% yield, ee = 88%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 5.173 min, t_{minor} = 6.023 min.). $[\alpha]_D^{20}$ = -103.8 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.71 (m, 4H), 7.51 (td, *J* = 5.7, 2.3 Hz, 4H), 7.38 (dd, *J* = 9.9, 6.8 Hz, 4H), 6.23 (s, 2H), 3.95 (t, *J* = 9.0 Hz, 1H), 3.65-3.46 (m, 3H), 1.48 (s, 9H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO) δ 168.36, 168.15, 162.54, 154.26, 132.96, 132.73, 131.91, 129.84, 129.29, 129.22, 128.07, 127.94, 127.74, 127.70, 126.94, 126.64, 119.07, 87.23, 85.09, 85.03, 80.48, 63.33, 53.53, 37.94, 28.34, 15.63, 13.52. HRMS (ESI) Calcd for $C_{32}H_{33}N_3O_5H^+$ $[M+H]^+$ 540.2493; Found: 540.2485.



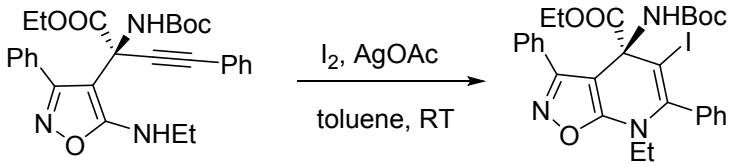
Ethyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(triisopropylsilyl) but-3-ynoate (3am): white solid, m.p.:119.3-123.4 °C, 54.7 mg, 96% yield, ee = 97%, HPLC conditions: Chiralpak OD-H (isopropyl alcohol/n-hexane: 1/99, 1.0 mL/min., t_{major} = 5.632 min., t_{minor} = 6.082 min.). $[\alpha]_D^{20}$ = -81.1 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.40 (m, 2H), 7.40-7.30 (m, 3H), 6.32 (s, 1H), 6.24 (s, 1H), 3.86-3.70 (m, 1H), 3.61-3.40 (m, 2H), 3.35 (s, 1H), 1.43 (s, 9H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.04 (s, 21H), 1.00 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.48, 168.13, 162.48, 153.98, 129.80, 129.22, 129.03, 128.03, 101.95, 86.80, 85.97, 80.04, 63.06, 53.12, 37.93, 28.27, 18.48, 15.49, 13.37, 11.11. HRMS (ESI) Calcd for $C_{31}H_{47}N_3O_5SiH^+$ $[M+H]^+$ 570.3358; Found: 570.3346.



Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-cyclopropyl-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3an): light yellow solid, m.p.: 95.2-98.7 °C, 44.9 g, 99% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (ethanol/n-hexane: 20/80, 1.0 mL/min., t_{major} = 4.365 min., t_{minor} = 6.665 min.). $[\alpha]_D^{20}$ = -59.9 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48-7.30 (m, 5H), 6.05 (s, 2H), 3.85 (dq, *J* = 14.1, 7.2 Hz, 1H), 3.59 – 3.39 (m, 3H), 1.42 (s, 9H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.18 (dt, *J* = 8.2, 5.0 Hz, 1H), 1.04 (t, *J* = 7.1 Hz, 3H), 0.79-0.70 (m, 2H), 0.61 (dt, *J* = 5.0, 3.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.25, 168.99, 163.21, 154.86, 130.71, 129.94, 128.75, 89.45, 88.27, 80.92, 71.53, 63.82, 53.64, 38.70, 29.10, 16.37, 14.23, 8.87, 0.11. HRMS (ESI) Calcd for $C_{25}H_{32}N_3O_5^+$ $[M+H]^+$ 454.2366; Found: 454.2330.

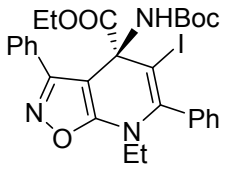
3. Transformations of the products

3.1 Iodocyclization of 3aa[4]



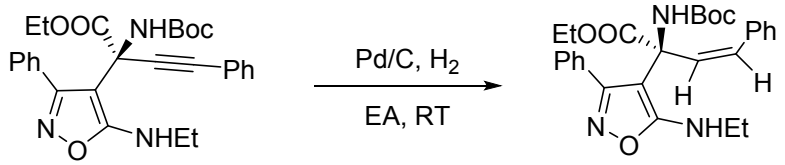
3aa, 96% ee **4**, 96% ee

In a vial was charged with **3aa** (49 mg, 0.1 mmol, 1 equiv, 96% ee), AgOAc (3.34 mg, 0.1 mmol, 0.2 equiv) and dry toluene (1 mL). A solution of I_2 (38 mg, 1.5 equiv.) dissolved in 0.5 mL of toluene was added dropwise. The reaction mixture was stirred at room temperature for 5 hours. The reaction mixture was then quenched with 10 mL of saturated aqueous $Na_2S_2O_3$ solution and extracted three times with ethyl ether. The combined organic layers were combined and dried over anhydrous anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by chromatography on silica gel using petroleum ether/EtOAc = 10/1 as eluent to afford compound **4** as a white solid (29 mg, 47% yield, 96%ee).



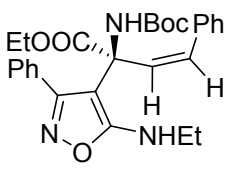
Ethyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-7-ethyl-5-iodo-3,6-diphenyl-4,7-dihydroisoxazolo[5,4-b]pyridine-4-carboxylate (4): white solid, m.p.: 138.5-140.7 °C, 47% yield, ee = 96%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 10/90, 1.0 mL/min., t_{major} = 3.975 min., t_{minor} = 5.032 min.). $[\alpha]_D^{20}$ = -42.1 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.55-7.50 (m, 8H), 7.33-7.20 (m, 2H), 6.43 (s, 1H), 4.00 (t, *J* = 7.1 Hz, 2H), 3.50 (t, *J* = 7.3 Hz, 2H), 1.37 (s, 9H), 1.03 (t, *J* = 7.0 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO) δ 169.39, 162.48, 160.58, 153.00, 142.36, 137.44, 130.14, 129.47, 129.25, 128.97, 128.71, 128.16, 128.09, 88.86, 79.12, 63.66, 62.95, 42.39, 28.22, 28.06, 14.47, 13.52.

3.2 Hydrogenation of alkyne moiety



3aa, 96% ee　　**5**, 93% ee

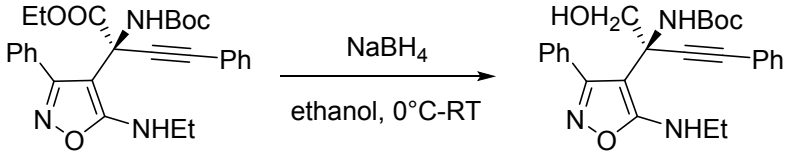
A solution of Pd/C (5wt%) and **3aa** (49 mg, 0.1 mmol, 1.0 equiv, 96% ee) in 1 mL of ethyl acetate was stirred at room temperature under hydrogen atmosphere using a balloon. The resulting mixture was filtered through celite pad and the pad was washed with ethyl acetate. After removal of the solvent, the mixture was purified by flash silica gel column chromatography using petroleum ether/EtOAc = 10/1 as eluent to give product **5** as a white solid (30 mg, 61% yield, 93% ee).



Ethyl (*S*,*Z*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-enoate (5): white solid, m.p.: 95.4-100.1 °C, 61% yield, ee = 93%, HPLC conditions: Chiralpak AD-H (isopropyl alcohol/n-hexane: 5/95, 1.0 mL/min., t_{major} = 6.357 min., t_{minor} = 7.792 min.). $[\alpha]_D^{20}$ = +46.1 (c 1.0, dichloromethane). ^{1}H NMR (400 MHz,

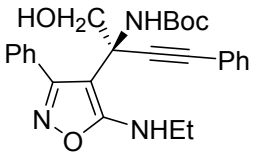
DMSO-d_6) δ 7.45-7.36 (m, 5H), 7.29-7.19 (m, 3H), 7.16-7.11 (m, 2H), 6.46 (d, *J* = 12.6 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H), 6.07 (t, *J* = 6.0 Hz, 1H), 5.94 (d, *J* = 12.5 Hz, 1H), 3.70-3.62 (m, 1H), 3.53 (s, 1H), 3.28 (t, *J* = 7.2 Hz, 2H), 1.16 (s, 9H), 1.16 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.26, 167.22, 162.64, 153.74, 135.97, 132.21, 130.78, 129.55, 129.52, 129.27, 128.41, 127.97, 127.50, 89.79, 79.07, 62.32, 59.19, 37.88, 28.31, 16.03, 13.86. HRMS (ESI) Calcd for $C_{28}H_{33}N_3O_5H^+$ $[M+H]^+$ 492.2493; Found: 492.2496.

3.3 Reduction of ester



3aa, 96% ee **6**, 95% ee

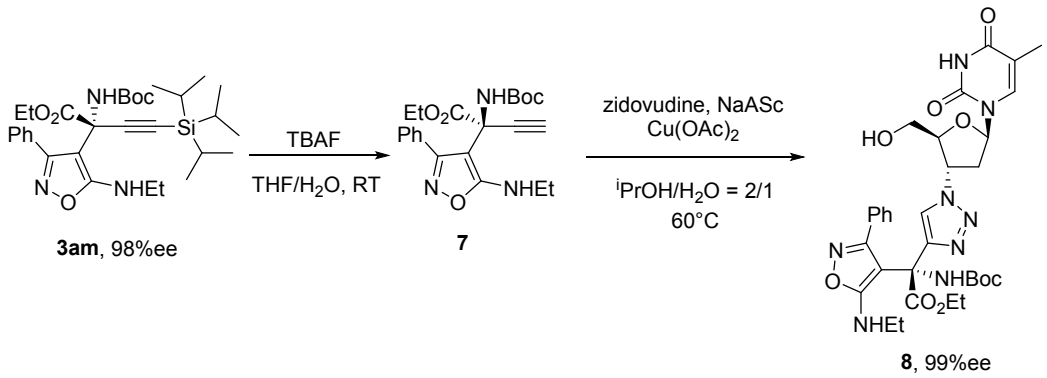
To a solution of $NaBH_4$ (11 mg, 0.3 mmol) in ethanol (1 mL) was added **3aa** (49 mg, 0.1 mmol, 96% ee) at 0 °C and the reaction mixture was stirred and warmed up to room temperature. The resulting mixture was then quenched with saturated aqueous NH_4Cl solution and the organic layer was separated. The organic layer was dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (Petroleum ether/EtOAc = 5/1) to gave the corresponding product **6** as a light yellow solid (31 mg, 69% yield, 95% ee).



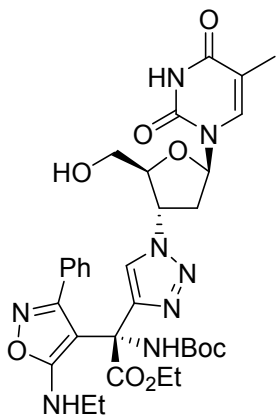
***tert*-butyl (*S*)-(2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-1-hydroxy-4-phenylbut-3-yn-2-yl)carbamate (6):** white solid, m.p.: 78.2–88.9 °C, 69% yield, ee = 95%, HPLC conditions: Chiralpak IC-H (isopropyl alcohol/n-hexane: 15/85, 1.0 mL/min., t_{major} = 14.769 min., t_{minor} = 11.000 min.). $[\alpha]_D^{20}$ = -10.5 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.46 (dd, *J* = 6.9, 2.9 Hz, 2H), 7.38-7.31 (m, 3H), 7.30-7.22 (m, 3H), 7.01 (s, 2H), 6.66 (s, 1H), 6.22 (t, *J* = 5.9 Hz, 1H), 5.58 (d, *J* = 6.4 Hz, 1H), 3.70 (m,

2H), 3.35-3.25 (q, 7.1 Hz, 2H), 1.26 (s, 9H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 166.13, 163.02, 153.70, 131.34, 131.23, 129.51, 129.17, 128.70, 128.53, 128.34, 127.64, 122.36, 89.77, 89.04, 83.59, 78.28, 67.80, 53.02, 37.44, 28.12, 15.67. HRMS (ESI) Calcd for $C_{26}H_{30}N_3O_4^+$ $[M+H]^+$ 448.2231; Found: 448.2229.

3.4 Click reaction[6]



Compound **3am** (57 mg, 0.1 mmol, 1 equiv., 98% ee) was dissolved in 20/1 THF/H_2O. Then tetrabutylammonium fluoride (TBAF, 31 mg, 0.12 mmol) was added and the solution stirred for 20 minutes at room temperature. Saturated aqueous NH_4Cl solution was added and the solution extracted with ethyl acetate, dried over Na_2SO_4, and evaporated under reduced pressure. No purification is required to proceed to the next step. To a solution of the zidovudine (26.7 mg, 0.1 mmol) and compound **7** (43 mg, 0.1 mmol) in 1mL *i*-PrOH/H_2O = 2/1 was added $Cu(OAc)_2$ (10 mol%) and sodium ascorbate (20 mol%) at 60 ^oC. After completion, water was added and the product was extracted with ethyl acetate. The organic layers were combined and dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. Purification by silica-gel chromatography (Petroleum ether/EtOAc = 1/1) to gave the corresponding product **8** as a white solid (55 mg, 81% yield, 99% ee).



Ethyl 2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-2-(1-((2*S*,3*S*,5*R*)-2-(hydroxymethyl)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl) tetrahydrofuran-3-yl)-1H-1,2,3-triazol-4-yl)acetate (8): white solid, m.p.: 148.7-157.6 °C, 81% yield, ee = 99%, HPLC conditions: Chiralpak AY-H (isopropyl alcohol /n-hexane: 20/80, 1.0 mL/min., t_{major} = 26.607 min., t_{minor} = 41.206 min.). $[\alpha]_D^{20}$ = -5.2 (c 1.0, dichloromethane). ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.34 (s, 1H), 8.07 (s, 1H), 7.87-7.68 (m, 1H), 7.47 (s, 1H), 7.37-7.08 (m, 5H), 6.34 (t, *J* = 6.6 Hz, 1H), 6.03 (s, 1H), 5.35-5.20 (m, 1H), 5.19-4.93 (m, 1H), 3.93 (d, *J* = 4.5 Hz, 1H), 3.89-3.71 (m, 2H), 3.71-3.59 (m, 1H), 3.58-3.45 (m, 1H), 3.32 (d, *J* = 9.1 Hz, 2H), 2.48 (s, 2H), 1.81 (s, 3H), 1.30 (s, 9H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 168.90, 167.15, 163.70, 162.61, 154.45, 150.41, 145.13, 136.17, 130.22, 128.80, 128.37, 127.43, 124.15, 109.61, 88.40, 84.24, 83.84, 79.07, 61.61, 60.69, 59.14, 57.80, 37.34, 36.90, 27.94, 15.44, 13.54, 12.19. HRMS (ESI) Calcd. for $C_{32}H_{40}N_8O_9Na^+$ $[M+Na]^+$ 703.2810; Found: 703.2836.

References

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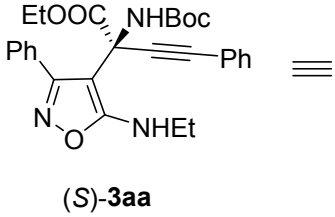
4. X-ray crystal structure of 3aa and 4

(a)X-ray crystal structure of **3aa**



(*S*)-**3aa**

≡

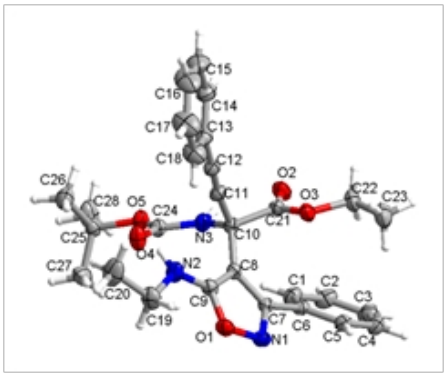


Table 1 Crystal data and structure refinement for 202012316.

Identification code	202012316
Empirical formula	C28H31N3O5
Formula weight	489.56
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	P212121
a/Å	8.5012(5)
b/Å	17.0320(7)
c/Å	18.9074(10)
α /°	90
β /°	90
γ /°	90
Volume/Å3	2737.7(2)
Z	4
ρ calcg/cm3	1.188
μ /mm-1	0.669
F(000)	1040.0
Crystal size/mm3	0.17 × 0.12 × 0.1
Radiation	CuKα (λ = 1.54184)

2Θ range for data collection/°	6.986 to 141.554
Index ranges	-8 ⩽ h ⩽ 10, -20 ⩽ k ⩽ 10, -22 ⩽ l ⩽ 21
Reflections collected	10617
Independent reflections	5157 [Rint = 0.0324, Rsigma = 0.0440]
Data/restraints/parameters	5157/5/355
Goodness-of-fit on F2	1.015
Final R indexes [I>=2σ (I)]	R1 = 0.0486, wR2 = 0.1219
Final R indexes [all data]	R1 = 0.0658, wR2 = 0.1393
Largest diff. peak/hole / e Å-3	0.21/-0.14
Flack parameter	-0.04(17)

Table 2 Fractional Atomic Coordinates (×104) and Equivalent Isotropic Displacement Parameters (Å2×103) for 202012316. Ueq is defined as 1/3 of of the trace of the orthogonalised UIJ tensor.

Atom	x	y	z	U(eq)
C1	6033(6)	4838(2)	584(2)	71.8(10)
C2	6763(7)	5338(3)	108(2)	87.6(14)
C3	7506(7)	5042(3)	-483(2)	90.8(14)
C4	7527(6)	4251(3)	-600(2)	81.6(12)
C5	6805(5)	3746(2)	-130(2)	70.8(10)
C6	6059(4)	4035(2)	469.8(18)	59.4(8)
C7	5281(4)	3500(2)	971.3(19)	58.0(8)
C8	5297(4)	3494.4(19)	1725.6(18)	54.8(7)
C9	4330(4)	2883.1(19)	1894(2)	62.0(8)
C10	6290(4)	3978.0(18)	2231.7(17)	53.9(7)
C11	6803(5)	3483(2)	2838.3(19)	63.1(9)
C12	7326(5)	3060(2)	3273.9(19)	67.9(9)
C13	7923(6)	2524(3)	3800(2)	77.1(11)

C14	9063(7)	2766(4)	4271(3)	99.3(16)
C15	9614(10)	2243(5)	4785(4)	132(3)
C16	9031(10)	1510(6)	4813(5)	158(4)
C17	7941(10)	1263(5)	4350(5)	150(3)
C18	7381(8)	1765(3)	3833(4)	112.5(19)
C19	2672(12)	1965(7)	2562(7)	92(3)
C19A	3160(50)	1860(30)	2670(40)	92(3)
C20	2362(14)	1775(5)	3315(5)	133(4)
C20A	1460(50)	2080(20)	2880(20)	133(4)
C21	7866(4)	4249(2)	1894(2)	62.7(9)
C22	10016(11)	3949(6)	1195(6)	87(2)
C22A	10331(15)	3637(8)	1488(7)	87(2)
C23	10532(15)	3254(7)	785(6)	123(3)
C23A	10520(20)	3928(11)	742(8)	123(3)
C24	4260(5)	4716(2)	2893.7(19)	61.1(8)
C25	2479(5)	5653(2)	3468(2)	68.4(9)
C26	2526(8)	5281(3)	4187(3)	102.8(16)
C27	1052(6)	5398(4)	3051(4)	115.7(19)
C28	2591(8)	6542(3)	3527(4)	117(2)
N1	4409(4)	2935(2)	707.9(18)	75.4(9)
N2	3853(5)	2578(2)	2514(2)	81.8(10)
N3	5535(4)	4701.0(17)	2468.7(17)	62.2(7)
O1	3786(3)	2531.9(15)	1308.3(16)	76.2(8)
O2	8327(4)	4909.2(18)	1939.0(19)	88.2(9)
O3	8599(3)	3659.6(18)	1595.3(16)	79.2(8)
O4	3553(4)	4138.9(14)	3088.1(19)	88.4(10)
O5	3913(3)	5460.9(13)	3059.7(15)	69.4(7)

Table 3 Anisotropic Displacement Parameters (Å2×103) for 202012316. The Anisotropic displacement factor exponent takes the form:

-2π2[h2a*2U11+2hka*b*U12+…].

Atom	U11	U22	U33	U23	U13	U12
C1	88(3)	66(2)	62(2)	2.2(17)	-2.2(19)	11(2)
C2	125(4)	63(2)	75(2)	11(2)	-10(3)	1(3)
C3	112(4)	96(3)	64(2)	18(2)	-1(3)	-12(3)
C4	96(3)	92(3)	58(2)	-1.3(19)	4(2)	5(3)
C5	76(3)	71(2)	64(2)	-2.9(18)	-3.8(19)	2.8(19)
C6	60(2)	62.3(18)	56.0(18)	1.0(15)	-10.7(16)	3.2(16)
C7	54.6(18)	56.0(18)	63.3(19)	-4.0(15)	-6.0(15)	1.6(15)
C8	52.5(16)	48.4(15)	63.5(19)	-4.7(14)	1.6(15)	1.3(14)
C9	61(2)	51.4(16)	74(2)	-4.6(16)	6.7(18)	-3.7(15)
C10	58.2(19)	48.0(15)	55.4(17)	-2.6(13)	2.7(15)	0.9(14)
C11	72(2)	58.9(18)	58.6(19)	-5.9(16)	-0.1(17)	1.8(18)
C12	78(2)	70(2)	56.3(19)	-1.2(17)	1.5(18)	11.2(19)
C13	84(3)	83(3)	64(2)	8.8(19)	4(2)	20(2)
C14	109(4)	115(4)	75(3)	-4(3)	-10(3)	24(3)
C15	115(5)	182(7)	97(4)	21(4)	-27(4)	16(5)
C16	132(6)	188(8)	155(7)	95(7)	-15(6)	28(6)
C17	135(6)	131(6)	184(8)	83(6)	-20(6)	-6(5)
C18	108(4)	95(4)	134(5)	36(3)	-10(4)	2(3)
C19	99(7)	67(4)	111(6)	9(4)	15(6)	-19(5)
C19A	99(7)	67(4)	111(6)	9(4)	15(6)	-19(5)
C20	178(9)	97(5)	125(7)	5(4)	49(7)	-50(6)
C20A	178(9)	97(5)	125(7)	5(4)	49(7)	-50(6)
C21	53.6(19)	69(2)	65(2)	-6.0(17)	-3.7(16)	-4.9(16)
C22	66(4)	94(6)	102(7)	13(4)	20(4)	13(4)
C22A	66(4)	94(6)	102(7)	13(4)	20(4)	13(4)
C23	93(5)	150(8)	125(6)	23(7)	34(5)	28(7)
C23A	93(5)	150(8)	125(6)	23(7)	34(5)	28(7)

C24	66(2)	49.2(17)	68(2)	-4.0(15)	5.3(17)	1.9(16)
C25	64(2)	63(2)	79(2)	-8.4(17)	7.8(19)	3.7(17)
C26	113(4)	114(4)	81(3)	1(3)	20(3)	15(4)
C27	74(3)	146(5)	127(4)	-32(4)	-9(3)	13(3)
C28	120(4)	70(3)	163(6)	-21(3)	46(4)	13(3)
N1	73(2)	78(2)	74(2)	-6.5(16)	-9.1(17)	-12.6(18)
N2	99(3)	63.9(18)	82(2)	-8.4(17)	20(2)	-25.0(19)
N3	69.4(19)	47.3(14)	70.0(17)	-4.2(13)	12.0(16)	-2.4(14)
O1	72.2(16)	66.8(14)	89.6(18)	-11.1(14)	-1.4(15)	-20.2(13)
O2	73.0(18)	82.7(19)	109(2)	-16.2(17)	8.6(17)	-29.2(15)
O3	57.5(14)	91.8(19)	88.3(18)	-14.9(15)	11.4(14)	-0.9(14)
O4	97(2)	51.5(14)	117(2)	-4.1(15)	43(2)	-6.2(14)
O5	76.0(17)	48.2(11)	83.9(16)	-7.4(12)	18.2(14)	1.2(11)

Table 4 Bond Lengths for 202012316.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C2	1.386(6)	C15	C16	1.344(11)
C1	C6	1.383(5)	C16	C17	1.342(12)
C2	C3	1.380(7)	C17	C18	1.383(8)
C3	C4	1.365(7)	C19	C20	1.484(15)
C4	C5	1.381(6)	C19	N2	1.452(12)
C5	C6	1.389(5)	C19A	C20A	1.54(3)
C6	C7	1.473(5)	C19A	N2	1.38(6)
C7	C8	1.426(5)	C21	O2	1.195(5)
C7	N1	1.312(5)	C21	O3	1.309(5)
C8	C9	1.364(5)	C22	C23	1.480(14)
C8	C10	1.518(5)	C22	O3	1.506(10)
C9	N2	1.344(5)	C22A	C23A	1.503(17)
C9	O1	1.341(5)	C22A	O3	1.486(12)

C10	C11	1.489(5)	C24	N3	1.350(5)
C10	C21	1.555(5)	C24	O4	1.209(4)
C10	N3	1.459(4)	C24	O5	1.340(4)
C11	C12	1.181(5)	C25	C26	1.501(6)
C12	C13	1.443(5)	C25	C27	1.511(7)
C13	C14	1.378(7)	C25	C28	1.520(6)
C13	C18	1.374(7)	C25	O5	1.479(5)
C14	C15	1.400(9)	N1	O1	1.429(4)

Table 5 Bond Angles for 202012316.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C6	C1	C2	119.9(4)	C16	C15	C14	119.7(7)
C3	C2	C1	120.5(4)	C17	C16	C15	121.3(7)
C4	C3	C2	119.8(4)	C16	C17	C18	120.4(8)
C3	C4	C5	120.3(4)	C13	C18	C17	119.8(7)
C4	C5	C6	120.5(4)	N2	C19	C20	109.8(9)
C1	C6	C5	119.0(4)	N2	C19A	C20A	104(3)
C1	C6	C7	120.3(3)	O2	C21	C10	122.2(3)
C5	C6	C7	120.7(3)	O2	C21	O3	126.6(4)
C8	C7	C6	130.1(3)	O3	C21	C10	111.1(3)
N1	C7	C6	117.6(3)	C23	C22	O3	103.8(8)
N1	C7	C8	112.3(3)	O3	C22A	C23A	103.0(11)
C7	C8	C10	129.2(3)	O4	C24	N3	124.4(3)
C9	C8	C7	103.5(3)	O4	C24	O5	126.1(3)
C9	C8	C10	127.0(3)	O5	C24	N3	109.5(3)
N2	C9	C8	132.9(4)	C26	C25	C27	111.9(5)
O1	C9	C8	110.8(3)	C26	C25	C28	110.6(4)
O1	C9	N2	116.3(3)	C27	C25	C28	112.0(5)
C8	C10	C21	112.4(3)	O5	C25	C26	110.9(4)
C11	C10	C8	109.9(3)	O5	C25	C27	109.0(3)

C11	C10	C21	103.4(3)	O5	C25	C28	102.0(4)
N3	C10	C8	114.0(3)	C7	N1	O1	105.1(3)
N3	C10	C11	111.8(3)	C9	N2	C19	122.8(6)
N3	C10	C21	104.8(3)	C9	N2	C19A	131(3)
C12	C11	C10	173.2(4)	C24	N3	C10	123.5(3)
C11	C12	C13	178.1(5)	C9	O1	N1	108.3(3)
C14	C13	C12	120.2(5)	C21	O3	C22	110.3(5)
C18	C13	C12	120.5(5)	C21	O3	C22A	123.4(6)
C18	C13	C14	119.3(5)	C24	O5	C25	120.9(3)
C13	C14	C15	119.5(6)				

Table 6 Hydrogen Bonds for 202012316.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
C1	H1	N3	0.93	2.87	3.596(5)	135.4
C4	H4	O11	0.93	2.83	3.488(5)	128.3
C5	H5	O11	0.93	2.94	3.541(5)	123.4
C20	H20C	O22	0.96	2.57	3.267(8)	129.2
C22A	H22C	O13	0.97	2.81	3.506(12)	129.6
C23	H23B	N13	0.96	2.51	3.343(12)	144.8
C28	H28A	O14	0.96	2.74	3.525(7)	140.0
N2	H2A	O4	0.85(2)	2.20(3)	2.882(4)	138(3)
N3	H3A	O2	0.86(2)	2.15(4)	2.601(4)	112(3)

11/2+X,1/2-Y,-Z; 21-X,-1/2+Y,1/2-Z; 31+X,+Y,+Z; 41-X,1/2+Y,1/2-Z

Table 7 Torsion Angles for 202012316.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C1	C2	C3	C4	-0.2(8)	C10	C21	O3	C22A	-154.6(7)
C1	C6	C7	C8	-44.2(6)	C11	C10	C21	O2	-108.3(4)
C1	C6	C7	N1	134.9(4)	C11	C10	C21	O3	69.0(4)
C2	C1	C6	C5	-0.9(6)	C11	C10	N3	C24	-57.5(5)

C2	C1	C6	C7	-179.8(4)	C12	C13	C14	C15	179.1(5)
C2	C3	C4	C5	0.2(8)	C12	C13	C18	C17	-178.6(6)
C3	C4	C5	C6	-0.5(7)	C13	C14	C15	C16	0.2(11)
C4	C5	C6	C1	0.8(6)	C14	C13	C18	C17	2.3(10)
C4	C5	C6	C7	179.7(4)	C14	C15	C16	C17	1.0(14)
C5	C6	C7	C8	136.9(4)	C15	C16	C17	C18	-0.5(15)
C5	C6	C7	N1	-44.0(5)	C16	C17	C18	C13	-1.2(13)
C6	C1	C2	C3	0.6(8)	C18	C13	C14	C15	-1.9(8)
C6	C7	C8	C9	178.1(4)	C20	C19	N2	C9	-178.0(7)
C6	C7	C8	C10	-8.6(6)	C20A	C19A	N2	C9	-110(4)
C6	C7	N1	O1	-178.6(3)	C21	C10	N3	C24	-168.8(3)
C7	C8	C9	N2	-179.5(4)	C23	C22	O3	C21	-169.8(7)
C7	C8	C9	O1	1.0(4)	C23A	C22A	O3	C21	-95.6(12)
C7	C8	C10	C11	-140.4(4)	C26	C25	O5	C24	62.0(5)
C7	C8	C10	C21	-25.8(5)	C27	C25	O5	C24	-61.7(5)
C7	C8	C10	N3	93.2(4)	C28	C25	O5	C24	179.8(4)
C7	N1	O1	C9	0.0(4)	N1	C7	C8	C9	-1.1(4)
C8	C7	N1	O1	0.7(4)	N1	C7	C8	C10	172.2(3)
C8	C9	N2	C19	173.4(6)	N2	C9	O1	N1	179.8(4)
C8	C9	N2	C19A	-164(2)	N3	C10	C21	O2	8.8(5)
C8	C9	O1	N1	-0.7(4)	N3	C10	C21	O3	-173.8(3)
C8	C10	C21	O2	133.2(4)	N3	C24	O5	C25	174.4(3)
C8	C10	C21	O3	-49.5(4)	O1	C9	N2	C19	-7.1(8)
C8	C10	N3	C24	68.0(5)	O1	C9	N2	C19A	16(2)
C9	C8	C10	C11	31.5(5)	O2	C21	O3	C22	-9.8(7)
C9	C8	C10	C21	146.0(4)	O2	C21	O3	C22A	22.5(9)
C9	C8	C10	N3	-94.9(4)	O4	C24	N3	C10	-4.6(6)
C10	C8	C9	N2	7.0(7)	O4	C24	O5	C25	-5.5(6)
C10	C8	C9	O1	-172.5(3)	O5	C24	N3	C10	175.5(3)

C10	C21	O3	C22	173.0(5)

Table 8 Hydrogen Atom Coordinates (Å×104) and Isotropic Displacement Parameters (Å2×103) for 202012316.

Atom	x	y	z	U(eq)
H1	5526	5041	980	86
H2	6752	5877	189	105
H3	7991	5381	-802	109
H4	8030	4052	-998	98
H5	6819	3208	-215	85
H14	9463	3274	4246	119
H15	10380	2401	5106	158
H16	9389	1167	5160	190
H17	7560	752	4377	180
H18	6640	1589	3507	135
H19A	3037	1499	2317	110
H19B	1707	2139	2337	110
H19C	3699	1610	3063	110
H19D	3173	1518	2267	110
H20A	2034	2241	3559	200
H20B	3304	1574	3529	200
H20C	1546	1386	3344	200
H20D	1468	2382	3310	200
H20E	856	1612	2949	200
H20F	991	2389	2510	200
H22A	9738	4379	883	105
H22B	10834	4122	1516	105
H22C	10735	3108	1539	105
H22D	10866	3979	1821	105

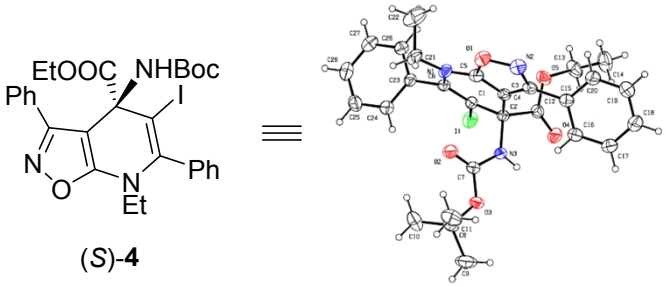
H23A	10529	2800	1086	184
H23B	11576	3341	608	184
H23C	9826	3171	396	184
H23D	11578	4105	672	184
H23E	9804	4355	661	184
H23F	10291	3509	418	184
H26A	2394	4724	4142	154
H26B	1694	5491	4473	154
H26C	3521	5390	4407	154
H27A	1086	5629	2588	174
H27B	115	5566	3290	174
H27C	1047	4836	3009	174
H28A	3497	6680	3803	176
H28B	1661	6741	3752	176
H28C	2685	6765	3062	176
H2A	3960(50)	2890(20)	2861(16)	62(11)
H3A	6060(50)	5129(18)	2410(20)	77(13)

Table 9 Atomic Occupancy for 202012316.

Atom	Occupancy	Atom	Occupancy	Atom	Occupancy
C19	0.807(12)	H19A	0.807(12)	H19B	0.807(12)
C19A	0.193(12)	H19C	0.193(12)	H19D	0.193(12)
C20	0.807(12)	H20A	0.807(12)	H20B	0.807(12)
H20C	0.807(12)	C20A	0.193(12)	H20D	0.193(12)
H20E	0.193(12)	H20F	0.193(12)	C22	0.571(7)
H22A	0.571(7)	H22B	0.571(7)	C22A	0.429(7)
H22C	0.429(7)	H22D	0.429(7)	C23	0.571(7)
H23A	0.571(7)	H23B	0.571(7)	H23C	0.571(7)
C23A	0.429(7)	H23D	0.429(7)	H23E	0.429(7)

H23F 0.429(7)

(b) X-ray crystal structure of 4



(*S*)-**4**

Table 1 Crystal data and structure refinement for 210410_s1_lm.

Identification code	210410_s1_lm
Empirical formula	C28H30IN3O5
Formula weight	615.45
Temperature/K	293.15
Crystal system	monoclinic
Space group	P21/c
a/Å	18.330(2)
b/Å	10.0441(6)
c/Å	16.8467(17)
α /°	90
β /°	116.711(13)
γ /°	90
Volume/Å3	2770.6(5)
Z	4
ρ calcg/cm3	1.475
μ /mm-1	1.197
F(000)	1248.0
Crystal size/mm3	0.35 × 0.3 × 0.25
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	6.036 to 52.742
Index ranges	-22 ⩽ h ⩽ 22, -10 ⩽ k ⩽12, -16 ⩽ l ⩽ 21
Reflections collected	14402
Independent reflections	5654 [Rint = 0.0273, Rsigma = 0.0407]
Data/restraints/parameters	5654/0/339
Goodness-of-fit on F2	1.036
Final R indexes [I>=2σ (I)]	R1 = 0.0463, wR2 = 0.1124
Final R indexes [all data]	R1 = 0.0686, wR2 = 0.1283
Largest diff. peak/hole / e Å-3	1.22/-1.22

Table 2 Fractional Atomic Coordinates (×104) and Equivalent Isotropic Displacement Parameters (Å2×103) for 210410_s1_lm. Ueq is defined as 1/3 of of the trace of the orthogonalised UIJ tensor.

Atom	x	y	z	U(eq)
I1	2954.7(2)	12367.2(3)	3361.7(2)	59.22(14)
O1	3630.7(17)	7838(3)	5976.4(18)	54.0(7)
O2	2293.2(17)	11107(3)	5517.9(18)	62.6(8)
O3	1007.3(16)	11716(3)	4548.3(19)	57.4(8)
O4	1506.9(17)	9636(3)	2515.5(18)	57.2(8)
O5	2760.7(17)	8751(3)	3058.4(18)	53.8(7)
N1	3961.7(18)	10003(4)	5757(2)	46.4(8)
N2	3012(2)	6879(4)	5494(2)	54.9(9)
N3	1727.1(19)	10556(3)	4057(2)	45.4(8)
C1	3142(2)	10916(4)	4325(2)	40.1(8)
C2	2451(2)	9924(4)	4069(2)	38.2(8)
C3	2769(2)	8805(4)	4719(2)	38.4(8)
C4	2519(2)	7480(4)	4757(3)	42.6(9)
C5	3456(2)	8942(4)	5485(2)	43.8(9)

C6	3788(2)	11018(4)	5125(2)	40.6(8)
C7	1734(2)	11129(4)	4787(3)	47.9(10)
C8	836(3)	12411(4)	5217(3)	61.0(13)
C9	-44(3)	12859(7)	4650(4)	97(2)
C10	1396(4)	13577(5)	5593(4)	84.6(17)
C11	878(4)	11435(6)	5915(4)	84.4(16)
C12	2168(2)	9419(4)	3111(2)	42.2(9)
C13	2611(3)	8244(5)	2191(3)	67.6(13)
C14	2327(4)	6871(6)	2069(4)	83.7(16)
C15	1820(2)	6722(4)	4103(3)	44.7(9)
C16	1059(3)	7311(4)	3647(4)	63.1(13)
C17	416(3)	6590(5)	3042(4)	86.0(18)
C18	513(3)	5291(5)	2881(4)	82.6(17)
C19	1258(3)	4705(5)	3320(4)	76.8(15)
C20	1912(3)	5411(4)	3926(3)	61.2(12)
C21	4563(2)	10114(5)	6698(3)	58.7(12)
C22	5347(3)	9372(7)	6879(4)	107(2)
C23	4350(2)	12168(4)	5418(3)	43.7(9)
C24	4101(3)	13335(4)	5657(3)	55.9(11)
C25	4615(3)	14408(5)	5937(3)	63.6(13)
C26	5382(3)	14331(5)	5989(3)	64.3(13)
C27	5633(3)	13182(5)	5747(3)	62.1(12)
C28	5120(2)	12100(4)	5464(3)	51.9(10)

Table 3 Anisotropic Displacement Parameters (Å2×103) for 210410_s1_lm. The Anisotropic displacement factor exponent takes the form: -2π2[h2a*2U11+2hka*b*U12+…].

Atom	U11	U22	U33	U23	U13	U12
I1	60.6(2)	52.1(2)	49.9(2)	7.49(13)	11.50(15)	-1.67(13)

O1	53.1(17)	66.9(18)	36.3(15)	12.2(14)	14.9(13)	5.1(15)
O2	47.5(17)	91(2)	40.5(16)	-15.1(16)	11.9(14)	16.9(16)
O3	45.0(15)	71(2)	51.4(17)	-14.4(15)	17.3(13)	17.9(15)
O4	48.7(16)	74(2)	36.3(15)	-5.3(14)	7.8(13)	3.1(15)
O5	62.7(18)	62.5(18)	40.7(15)	-7.1(14)	27.1(14)	12.0(14)
N1	36.3(17)	62(2)	33.0(17)	-1.0(16)	8.8(14)	2.2(15)
N2	57(2)	60(2)	50(2)	10.4(19)	26.1(18)	3.0(18)
N3	32.7(16)	56.2(19)	39.5(18)	-10.2(15)	9.3(14)	8.4(15)
C1	37.7(19)	42(2)	36(2)	-2.5(16)	12.3(16)	4.0(16)
C2	33.6(18)	46(2)	33.2(19)	-3.4(16)	13.9(16)	6.0(16)
C3	38.9(19)	45(2)	32.2(19)	0.4(16)	16.4(16)	8.6(16)
C4	45(2)	52(2)	39(2)	4.0(18)	25.7(18)	9.0(17)
C5	46(2)	55(2)	33(2)	6.1(18)	19.8(17)	9.5(19)
C6	34.6(19)	49(2)	38(2)	-4.1(17)	15.9(16)	5.3(16)
C7	40(2)	52(2)	51(2)	-7(2)	19.2(19)	7.1(18)
C8	58(3)	66(3)	59(3)	-9(2)	27(2)	21(2)
C9	71(4)	121(5)	97(5)	-5(4)	37(3)	47(3)
C10	109(4)	65(3)	87(4)	-26(3)	51(4)	-5(3)
C11	97(4)	85(4)	90(4)	5(3)	59(4)	19(3)
C12	48(2)	43(2)	37(2)	-2.5(17)	19.6(19)	1.1(17)
C13	94(4)	74(3)	48(3)	-12(2)	43(3)	8(3)
C14	104(4)	87(4)	65(3)	-27(3)	42(3)	-18(3)
C15	46(2)	49(2)	45(2)	3.0(19)	26.0(18)	1.6(19)
C16	50(3)	53(3)	85(4)	-11(2)	29(3)	4(2)
C17	47(3)	68(3)	119(5)	-22(3)	17(3)	8(2)
C18	53(3)	68(3)	108(4)	-19(3)	20(3)	-7(3)
C19	71(3)	52(3)	97(4)	-15(3)	28(3)	2(2)
C20	53(3)	51(3)	70(3)	-1(2)	19(2)	5(2)
C21	48(2)	88(3)	29(2)	1(2)	7.4(18)	1(2)

C22	69(4)	153(6)	77(4)	28(4)	14(3)	16(4)
C23	36(2)	54(2)	35(2)	-5.8(18)	10.6(16)	1.6(17)
C24	47(2)	63(3)	53(3)	-11(2)	18(2)	4(2)
C25	72(3)	56(3)	50(3)	-11(2)	15(2)	6(2)
C26	66(3)	61(3)	50(3)	-3(2)	13(2)	-15(2)
C27	43(2)	75(3)	62(3)	4(3)	18(2)	-6(2)
C28	45(2)	57(2)	49(2)	-3(2)	16.1(19)	6(2)

Table 4 Bond Lengths for 210410_s1_lm.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
I1	C1	2.092(4)	C3	C5	1.346(5)
O1	N2	1.430(5)	C4	C15	1.471(6)
O1	C5	1.334(5)	C6	C23	1.477(5)
O2	C7	1.197(4)	C8	C9	1.526(7)
O3	C7	1.343(4)	C8	C10	1.498(7)
O3	C8	1.474(5)	C8	C11	1.505(7)
O4	C12	1.195(4)	C13	C14	1.455(8)
O5	C12	1.313(4)	C15	C16	1.387(6)
O5	C13	1.453(5)	C15	C20	1.377(6)
N1	C5	1.350(5)	C16	C17	1.368(7)
N1	C6	1.403(5)	C17	C18	1.360(7)
N1	C21	1.472(5)	C18	C19	1.360(7)
N2	C4	1.310(5)	C19	C20	1.372(6)
N3	C2	1.462(5)	C21	C22	1.523(7)
N3	C7	1.354(5)	C23	C24	1.382(6)
C1	C2	1.513(5)	C23	C28	1.379(6)
C1	C6	1.340(5)	C24	C25	1.369(6)
C2	C3	1.493(5)	C25	C26	1.370(7)
C2	C12	1.542(5)	C26	C27	1.370(7)

C3	C4	1.418(5)	C27	C28	1.375(6)

Table 5 Bond Angles for 210410_s1_lm.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C5	O1	N2	107.4(3)	O2	C7	N3	125.5(4)
C7	O3	C8	120.2(3)	O3	C7	N3	108.2(3)
C12	O5	C13	117.3(3)	O3	C8	C9	100.9(4)
C5	N1	C6	115.4(3)	O3	C8	C10	110.6(4)
C5	N1	C21	119.5(3)	O3	C8	C11	109.6(4)
C6	N1	C21	124.5(3)	C10	C8	C9	111.4(4)
C4	N2	O1	105.2(3)	C10	C8	C11	113.2(5)
C7	N3	C2	122.3(3)	C11	C8	C9	110.5(5)
C2	C1	I1	114.4(2)	O4	C12	O5	126.4(4)
C6	C1	I1	119.3(3)	O4	C12	C2	123.8(4)
C6	C1	C2	125.8(3)	O5	C12	C2	109.8(3)
N3	C2	C1	110.9(3)	O5	C13	C14	111.6(4)
N3	C2	C3	112.9(3)	C16	C15	C4	121.0(4)
N3	C2	C12	104.6(3)	C20	C15	C4	120.5(4)
C1	C2	C12	111.1(3)	C20	C15	C16	118.6(4)
C3	C2	C1	106.6(3)	C17	C16	C15	120.1(4)
C3	C2	C12	110.9(3)	C18	C17	C16	120.7(5)
C4	C3	C2	135.4(3)	C17	C18	C19	119.7(5)
C5	C3	C2	121.0(3)	C18	C19	C20	120.6(5)
C5	C3	C4	103.6(3)	C19	C20	C15	120.3(4)
N2	C4	C3	112.1(4)	N1	C21	C22	111.2(4)
N2	C4	C15	118.0(4)	C24	C23	C6	119.2(4)
C3	C4	C15	129.9(3)	C28	C23	C6	121.5(4)
O1	C5	N1	120.6(3)	C28	C23	C24	119.3(4)

O1	C5	C3	111.7(4)	C25	C24	C23	120.1(4)
C3	C5	N1	127.6(4)	C24	C25	C26	120.4(4)
N1	C6	C23	115.3(3)	C27	C26	C25	120.0(4)
C1	C6	N1	120.3(4)	C26	C27	C28	120.0(4)
C1	C6	C23	124.3(4)	C27	C28	C23	120.2(4)
O2	C7	O3	126.3(4)				

Table 6 Torsion Angles for 210410_s1_lm.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
I1	C1	C2	N3	-70.0(3)	C5	N1	C6	C23	-178.9(3)
I1	C1	C2	C3	166.8(2)	C5	N1	C21	C22	86.1(5)
I1	C1	C2	C12	45.9(4)	C5	C3	C4	N2	0.9(4)
I1	C1	C6	N1	-175.0(3)	C5	C3	C4	C15	-178.1(4)
I1	C1	C6	C23	6.1(5)	C6	N1	C5	O1	170.0(3)
O1	N2	C4	C3	-0.5(4)	C6	N1	C5	C3	-7.0(6)
O1	N2	C4	C15	178.6(3)	C6	N1	C21	C22	-103.1(5)
N1	C6	C23	C24	-103.0(4)	C6	C1	C2	N3	102.1(4)
N1	C6	C23	C28	76.5(5)	C6	C1	C2	C3	-21.2(5)
N2	O1	C5	N1	-176.8(3)	C6	C1	C2	C12	-142.1(4)
N2	O1	C5	C3	0.7(4)	C6	C23	C24	C25	179.5(4)
N2	C4	C15	C16	139.2(4)	C6	C23	C28	C27	-179.4(4)
N2	C4	C15	C20	-41.2(6)	C7	O3	C8	C9	-178.4(4)
N3	C2	C3	C4	74.0(5)	C7	O3	C8	C10	63.6(5)
N3	C2	C3	C5	-106.3(4)	C7	O3	C8	C11	-61.9(6)
N3	C2	C12	O4	5.1(5)	C7	N3	C2	C1	-60.1(5)
N3	C2	C12	O5	-175.9(3)	C7	N3	C2	C3	59.5(5)
C1	C2	C3	C4	-164.1(4)	C7	N3	C2	C12	-179.9(4)
C1	C2	C3	C5	15.7(4)	C8	O3	C7	O2	-0.6(7)
C1	C2	C12	O4	-114.5(4)	C8	O3	C7	N3	179.2(4)

C1	C2	C12	O5	64.4(4)	C12	O5	C13	C14	-94.8(5)
C1	C6	C23	C24	76.0(5)	C12	C2	C3	C4	-43.0(6)
C1	C6	C23	C28	-104.5(5)	C12	C2	C3	C5	136.7(4)
C2	N3	C7	O2	-5.4(7)	C13	O5	C12	O4	1.2(6)
C2	N3	C7	O3	174.8(3)	C13	O5	C12	C2	-177.7(3)
C2	C1	C6	N1	13.4(6)	C15	C16	C17	C18	0.3(9)
C2	C1	C6	C23	-165.5(3)	C16	C15	C20	C19	-0.9(7)
C2	C3	C4	N2	-179.3(4)	C16	C17	C18	C19	-0.6(10)
C2	C3	C4	C15	1.7(7)	C17	C18	C19	C20	0.2(10)
C2	C3	C5	O1	179.3(3)	C18	C19	C20	C15	0.6(8)
C2	C3	C5	N1	-3.5(6)	C20	C15	C16	C17	0.4(8)
C3	C2	C12	O4	127.1(4)	C21	N1	C5	O1	-18.4(5)
C3	C2	C12	O5	-53.9(4)	C21	N1	C5	C3	164.6(4)
C3	C4	C15	C16	-41.8(6)	C21	N1	C6	C1	-169.0(4)
C3	C4	C15	C20	137.8(4)	C21	N1	C6	C23	10.0(5)
C4	C3	C5	O1	-0.9(4)	C23	C24	C25	C26	-0.6(7)
C4	C3	C5	N1	176.3(4)	C24	C23	C28	C27	0.1(6)
C4	C15	C16	C17	-180.0(5)	C24	C25	C26	C27	1.2(7)
C4	C15	C20	C19	179.5(4)	C25	C26	C27	C28	-1.0(7)
C5	O1	N2	C4	-0.1(4)	C26	C27	C28	C23	0.4(7)
C5	N1	C6	C1	2.1(5)	C28	C23	C24	C25	0.0(6)

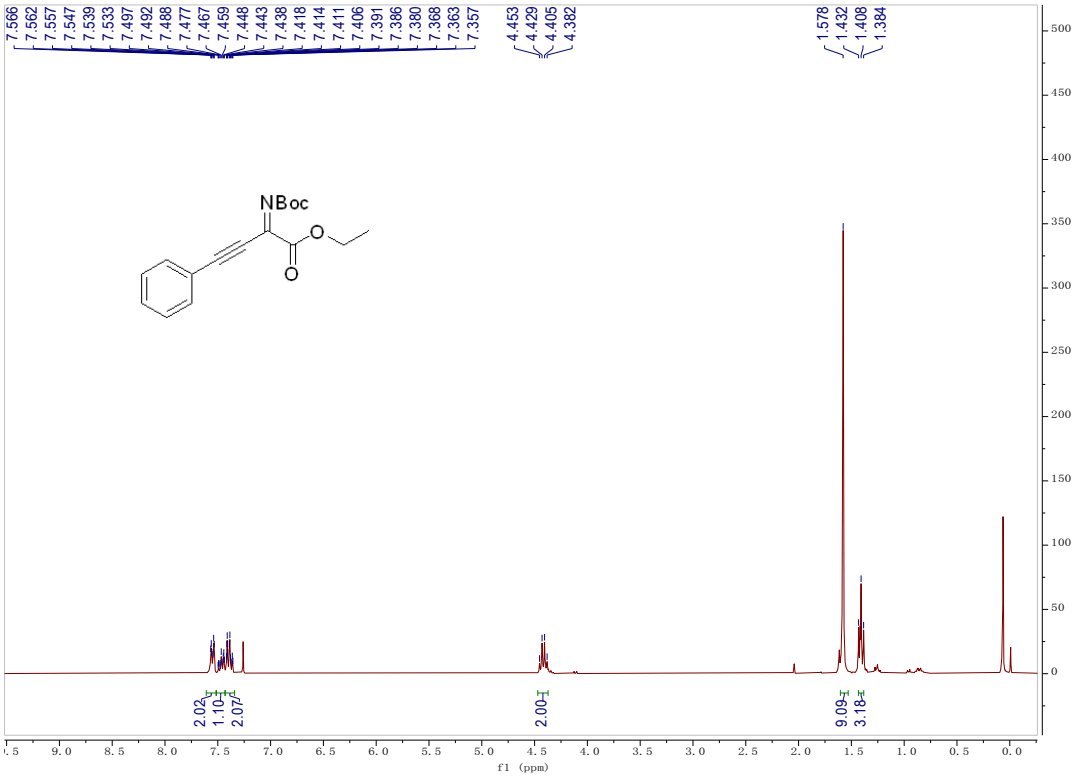
Table 7 Hydrogen Atom Coordinates (Å×104) and Isotropic Displacement Parameters (Å2×103) for 210410_s1_lm.

Atom	x	y	z	U(eq)
H3	1281.59	10563.51	3568.34	54
H9A	-61.12	13473.19	4205.43	145
H9B	-246.28	13286.15	5021.02	145
H9C	-376.56	12098.18	4367.19	145

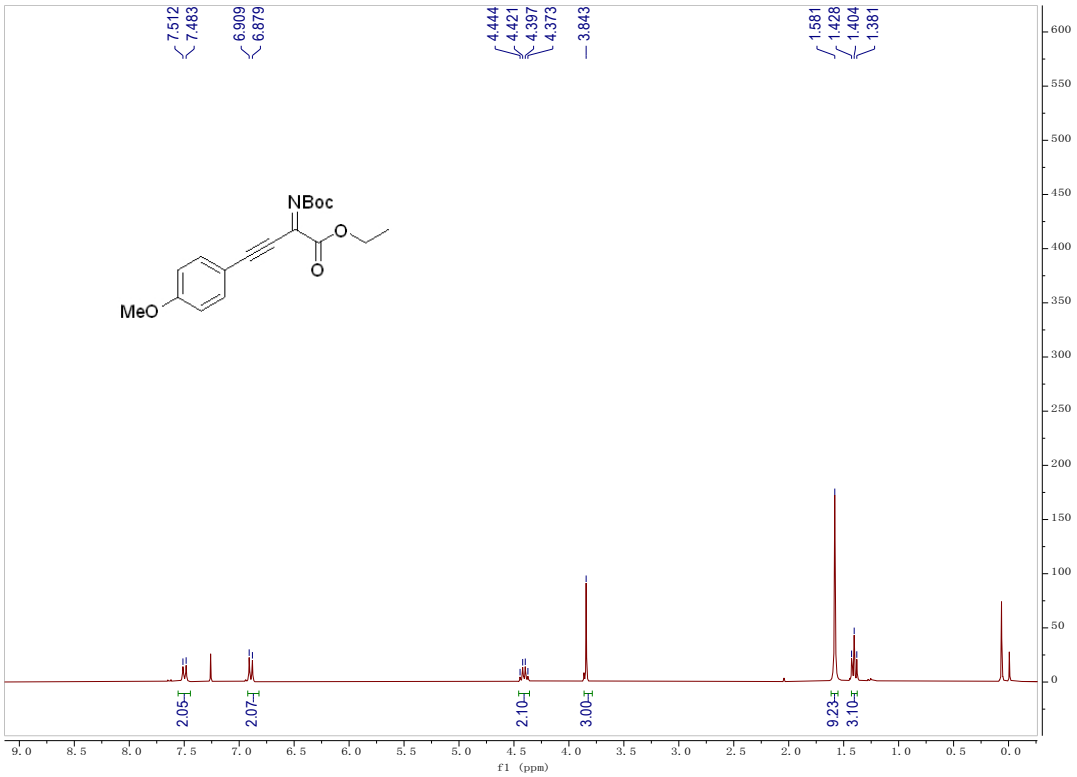
H10A	1948.93	13267.35	5910.17	127
H10B	1248.29	14057.34	5992.19	127
H10C	1350.89	14153.84	5118.97	127
H11A	525.52	10693.57	5633.74	127
H11B	706.61	11864.62	6311.78	127
H11C	1429.36	11124.68	6243.54	127
H13A	3110.3	8295.05	2127.79	81
H13B	2203.8	8794.92	1732.74	81
H14A	2252.44	6557.18	1499.54	125
H14B	1816.71	6825.07	2099.49	125
H14C	2723.75	6326.07	2528.23	125
H16	984.55	8197.21	3753.58	76
H17	-92.05	6992.1	2736.55	103
H18	71.73	4805.75	2472.24	99
H19	1324.29	3817.55	3209.21	92
H20	2419.46	5002.8	4218.05	73
H21A	4332.46	9750	7068.72	70
H21B	4686.92	11045.65	6851.37	70
H22A	5519.62	9609.39	6437.11	160
H22B	5250.64	8430.71	6856.69	160
H22C	5765.57	9609.83	7456.72	160
H24	3582.86	13390.73	5628.74	67
H25	4443.13	15194.28	6091.74	76
H26	5732.37	15057.74	6190	77
H27	6150.11	13135	5773.66	75
H28	5291.77	11319.82	5302.3	62

5. ^{1}H NMR and ^{13}C NMR spectra

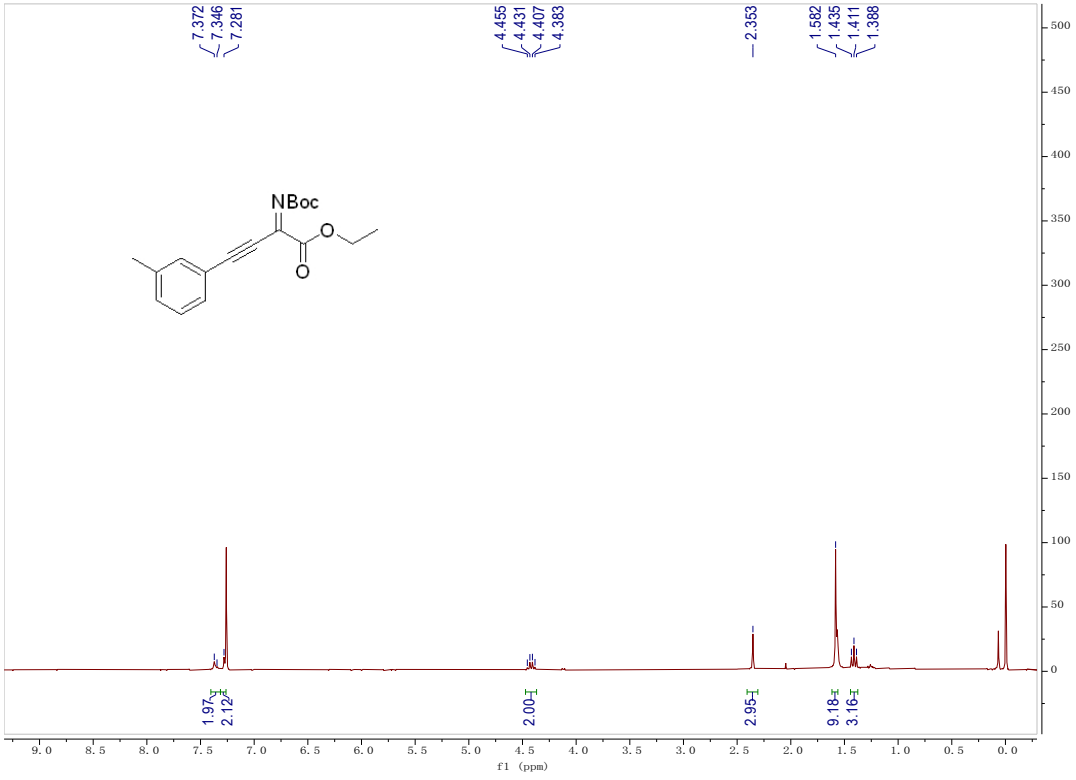
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-phenylbut-3-ynoate (2a)



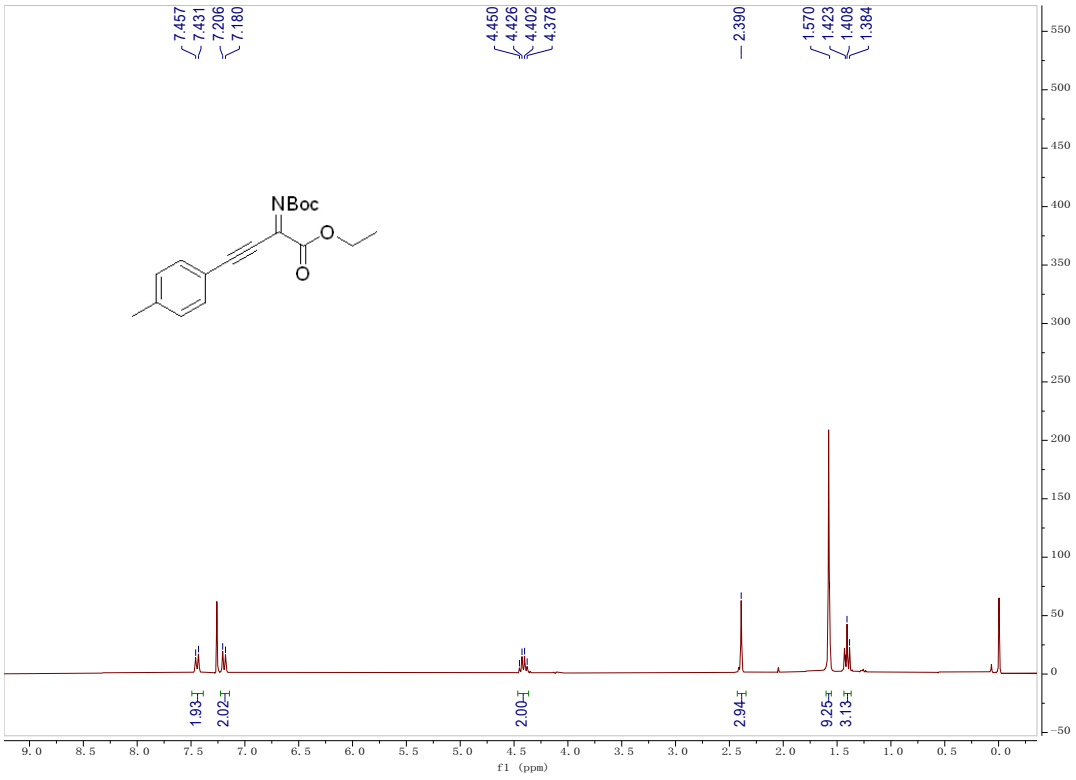
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-methoxyphenyl)but-3-ynoate (2b)



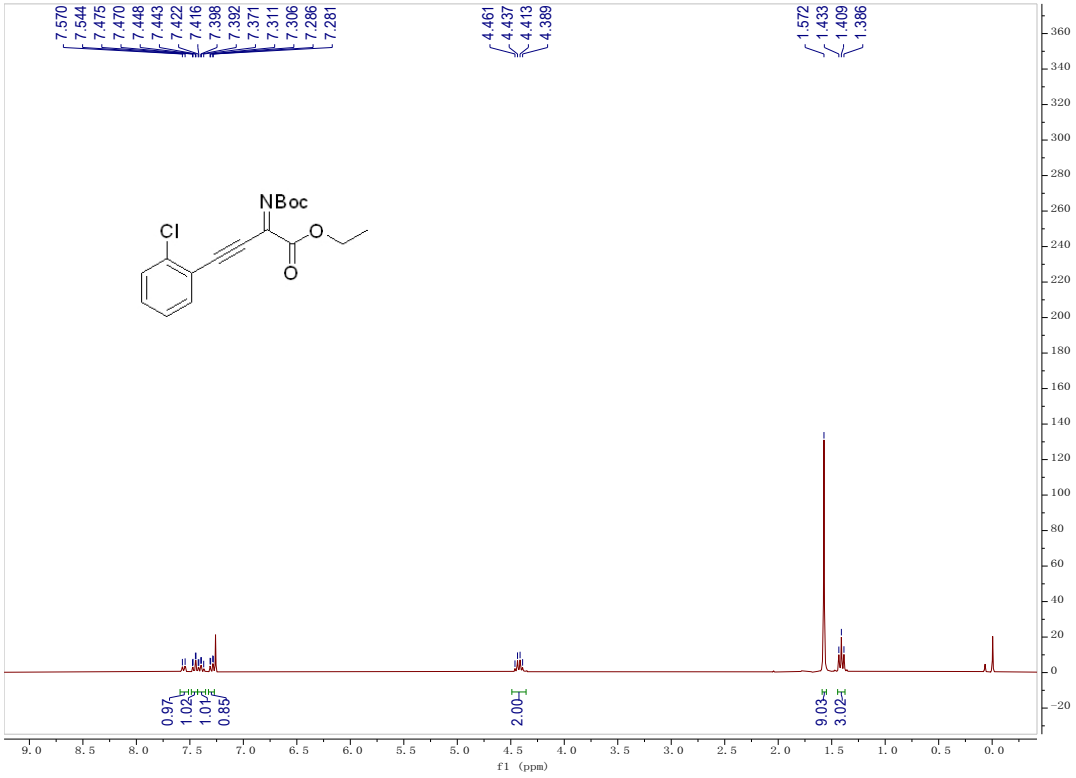
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(m-tolyl)but-3-ynoate (2c)



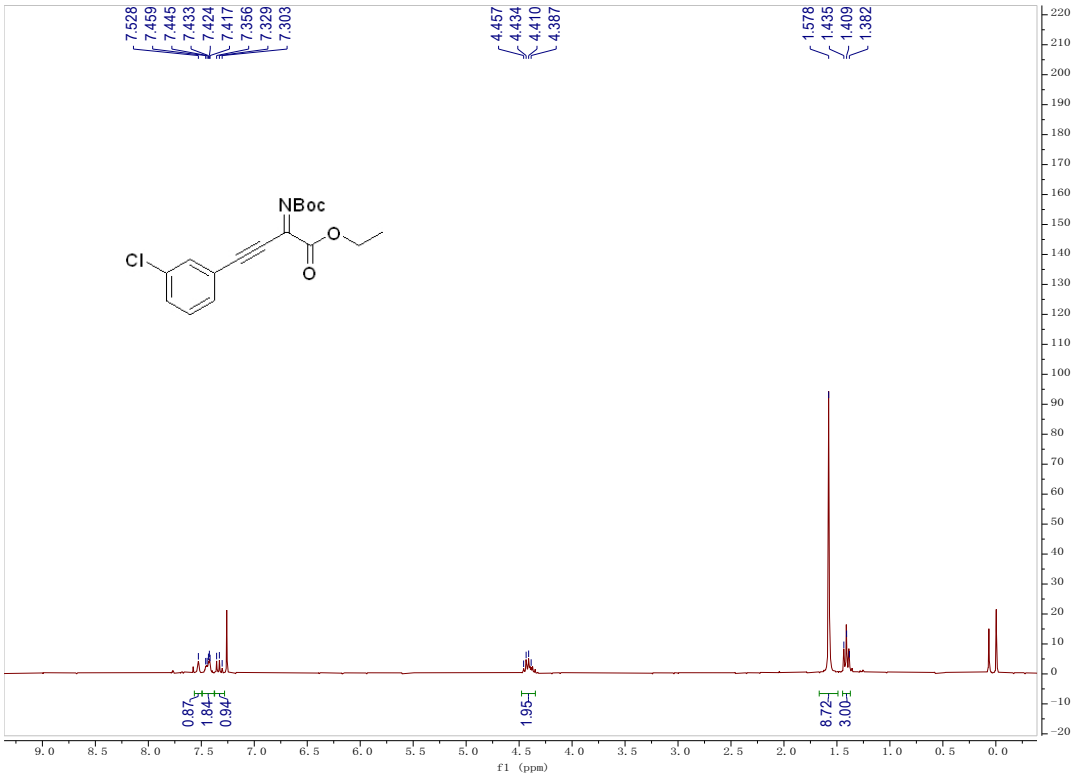
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(*p*-tolyl)but-3-ynoate (2d)



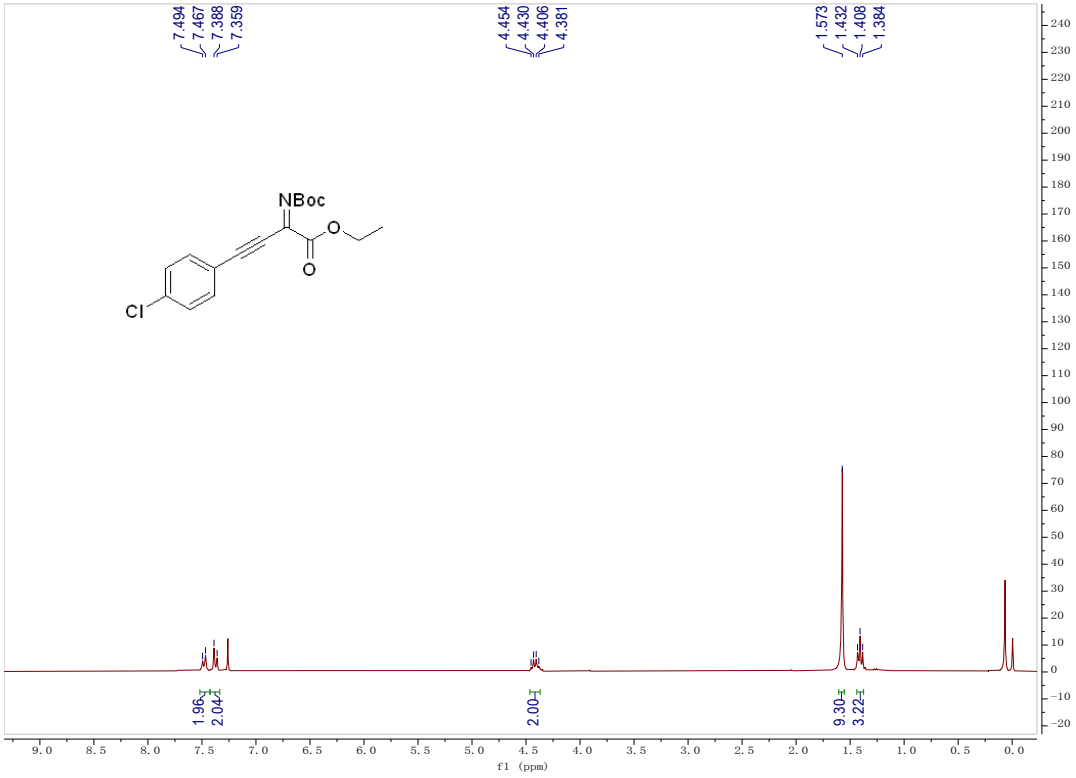
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(2-chlorophenyl)but-3-ynoate (2e)



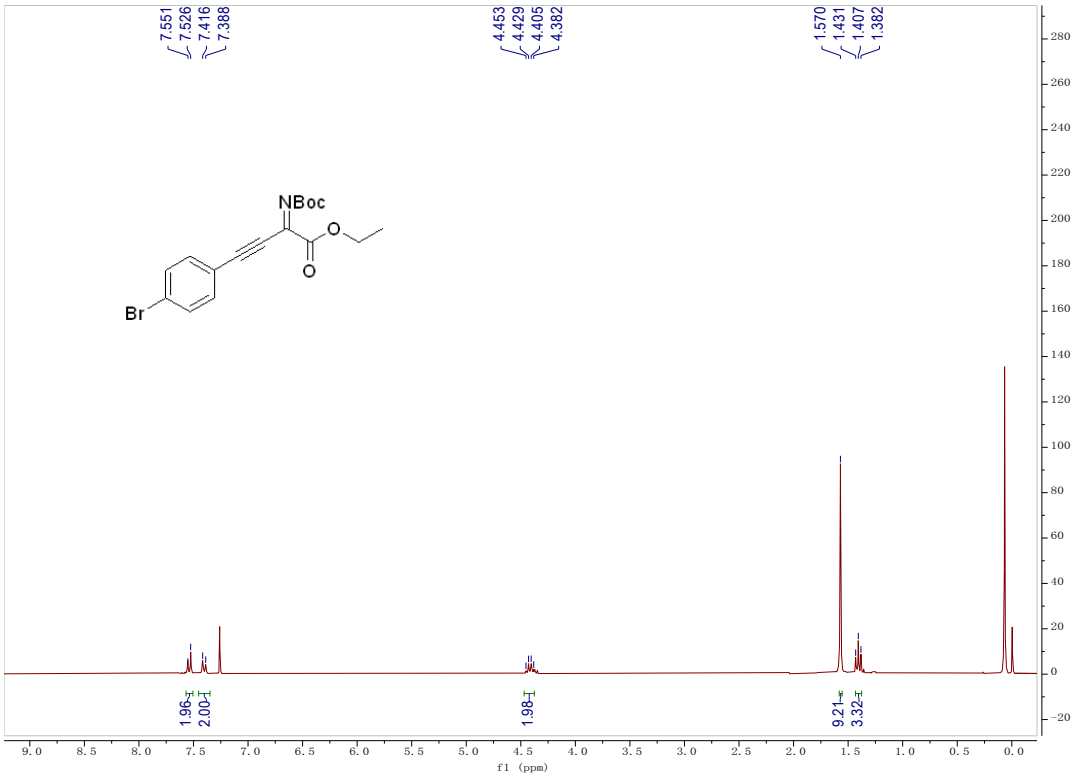
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(3-chlorophenyl)but-3-ynoate (2f)



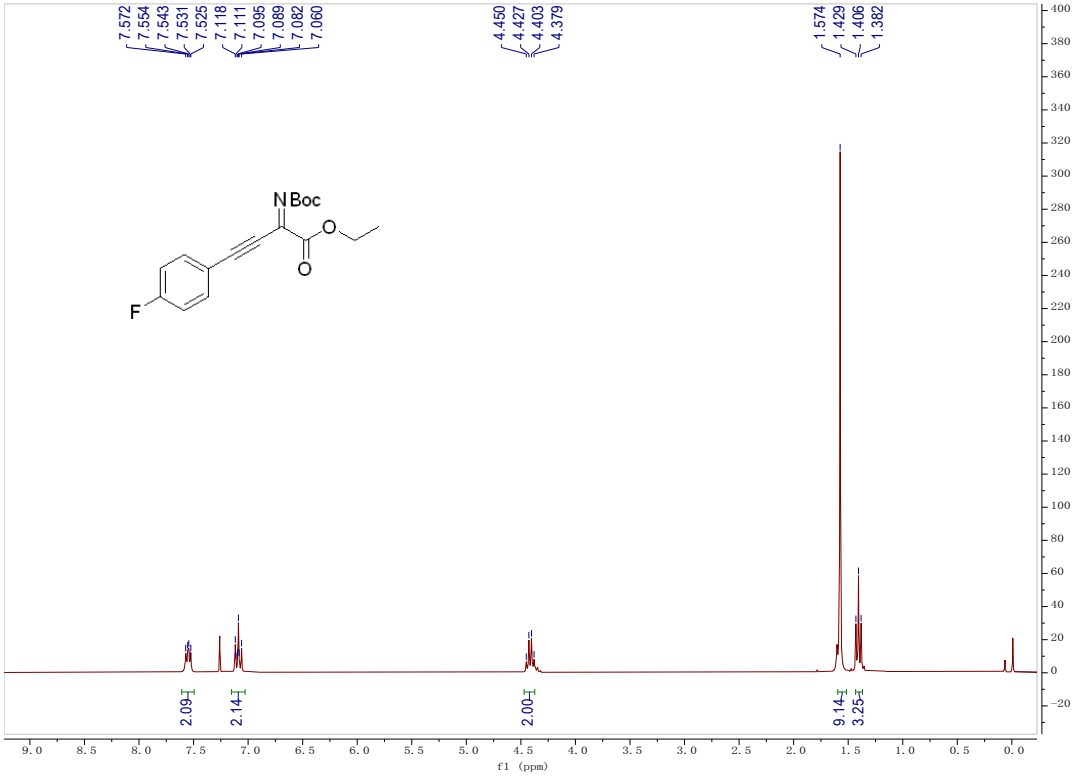
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-chlorophenyl)but-3-ynoate (2g)



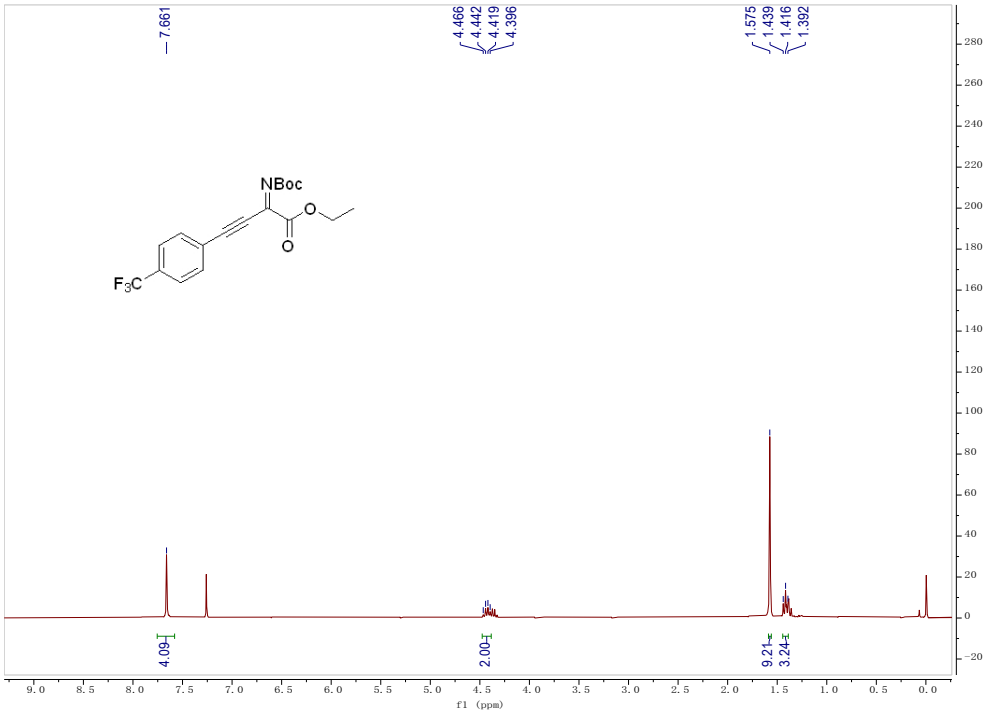
Ethyl (*E*)-4-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)imino)but-3-ynoate (2h)



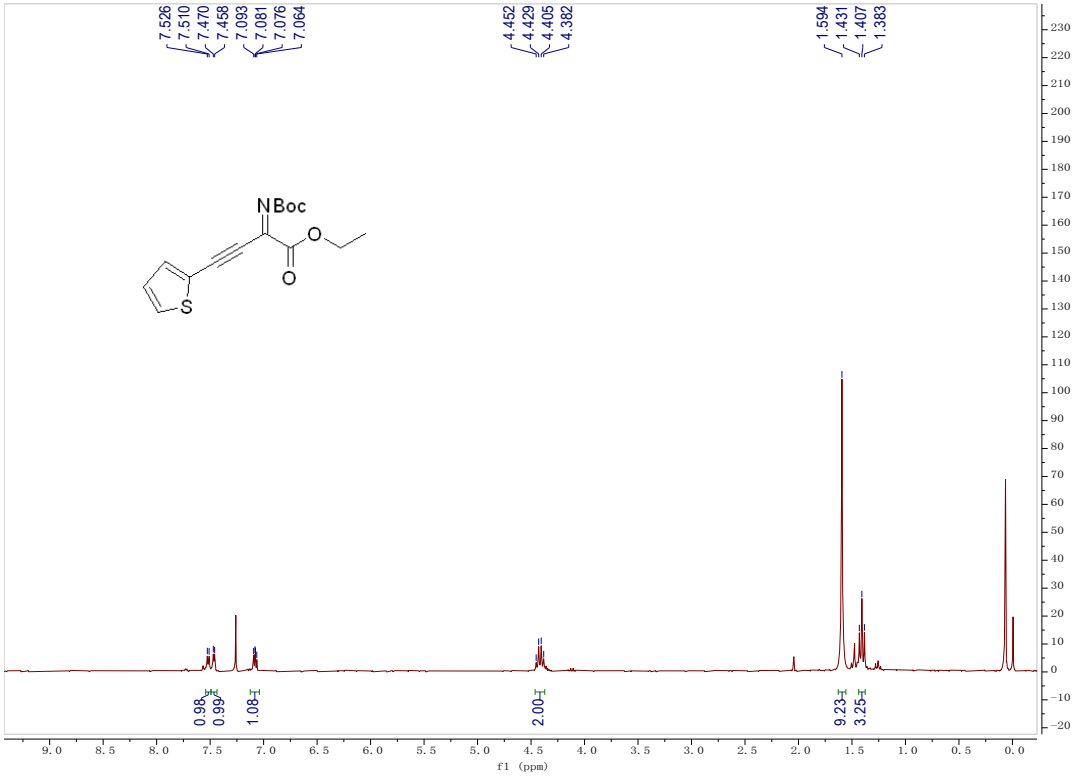
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-fluorophenyl)but-3-ynoate (2i)



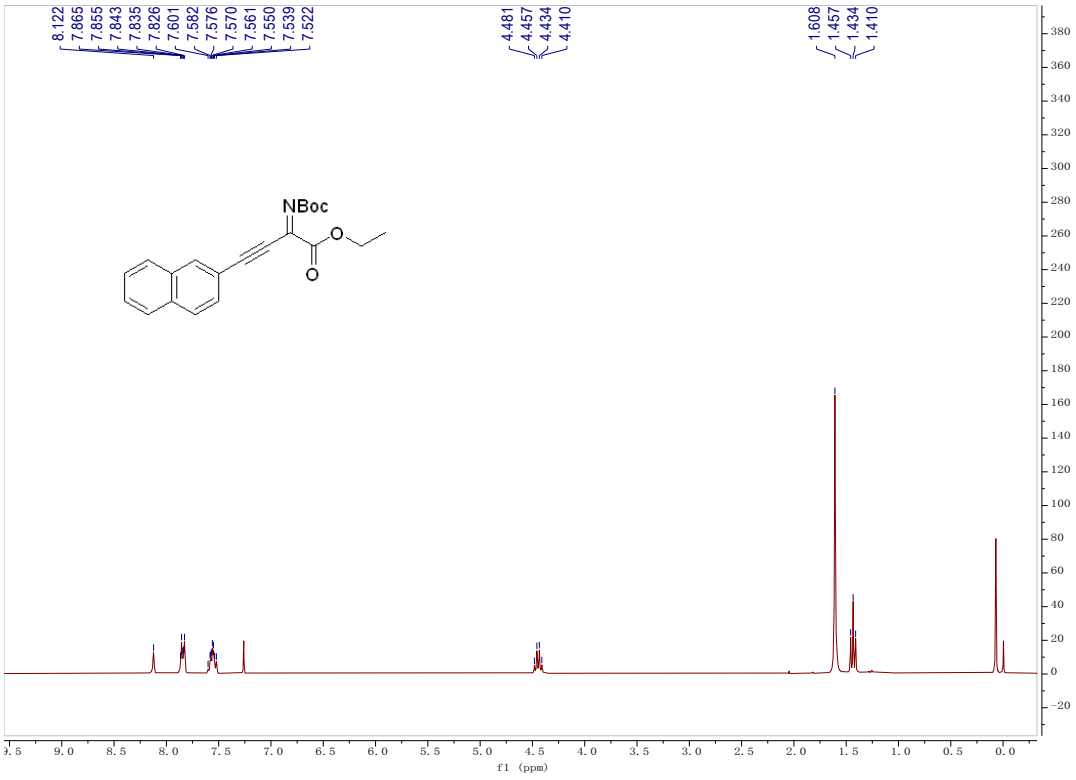
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(4-(trifluoromethyl)phenyl)but-3-ynoate (2j)



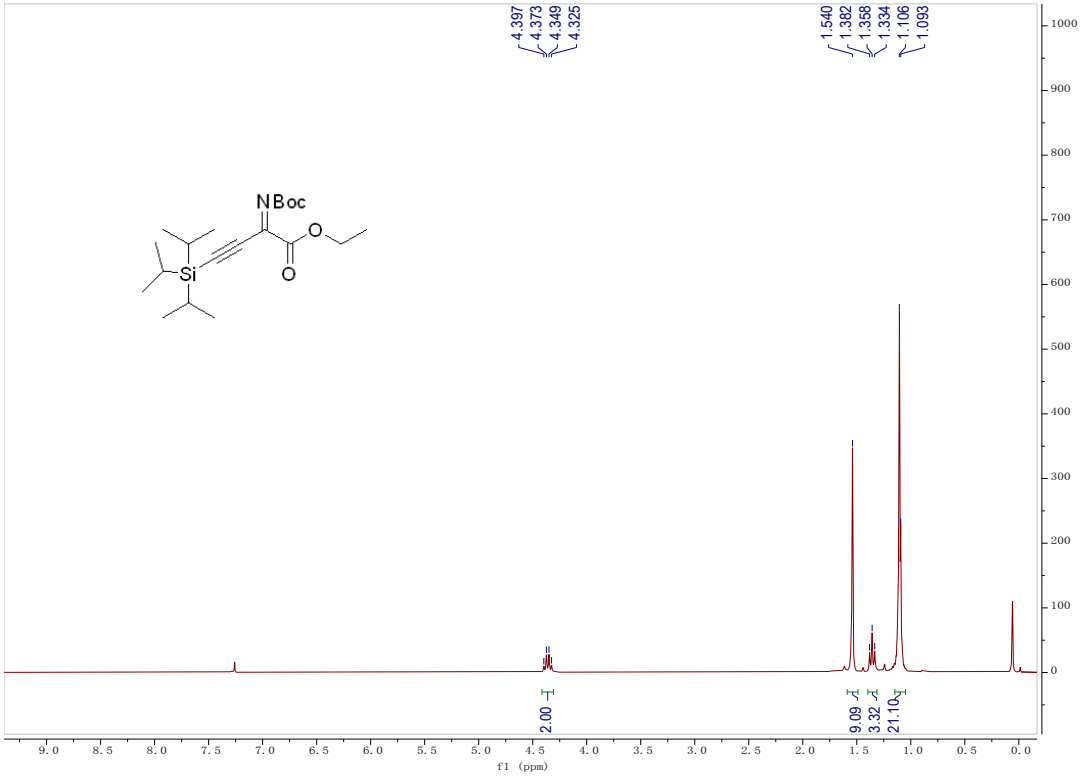
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(thiophen-2-yl)but-3-ynoate (2k)



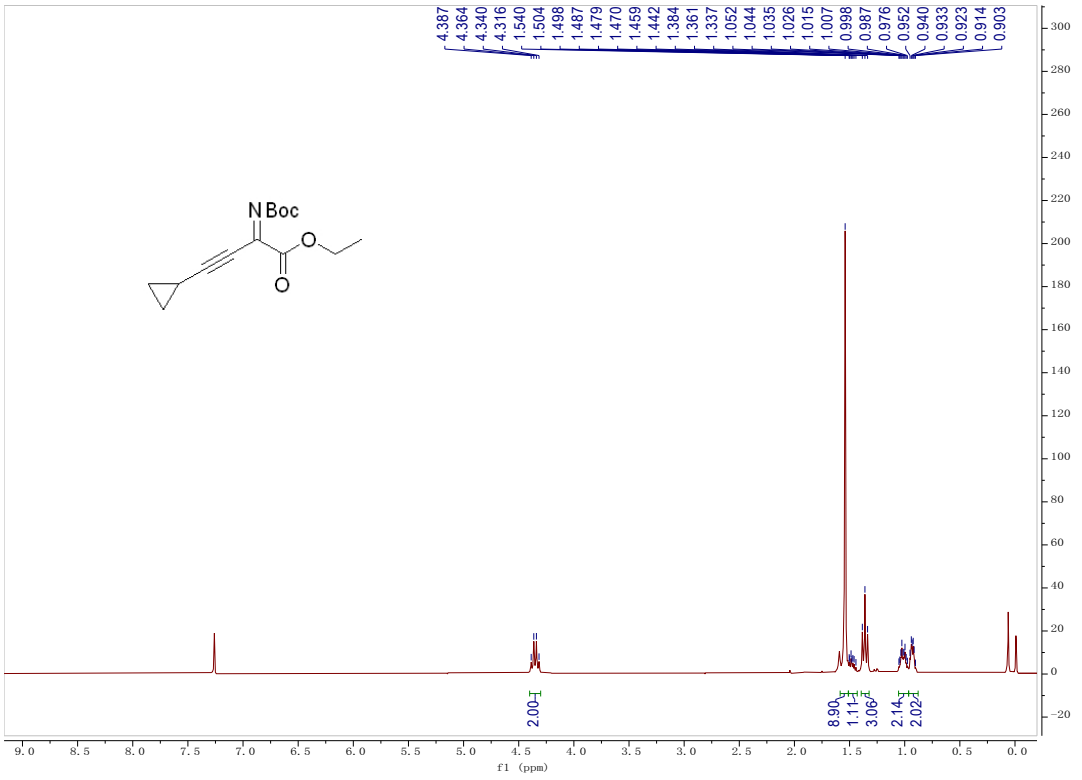
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(naphthalen-2-yl)but-3-ynoate (2l)



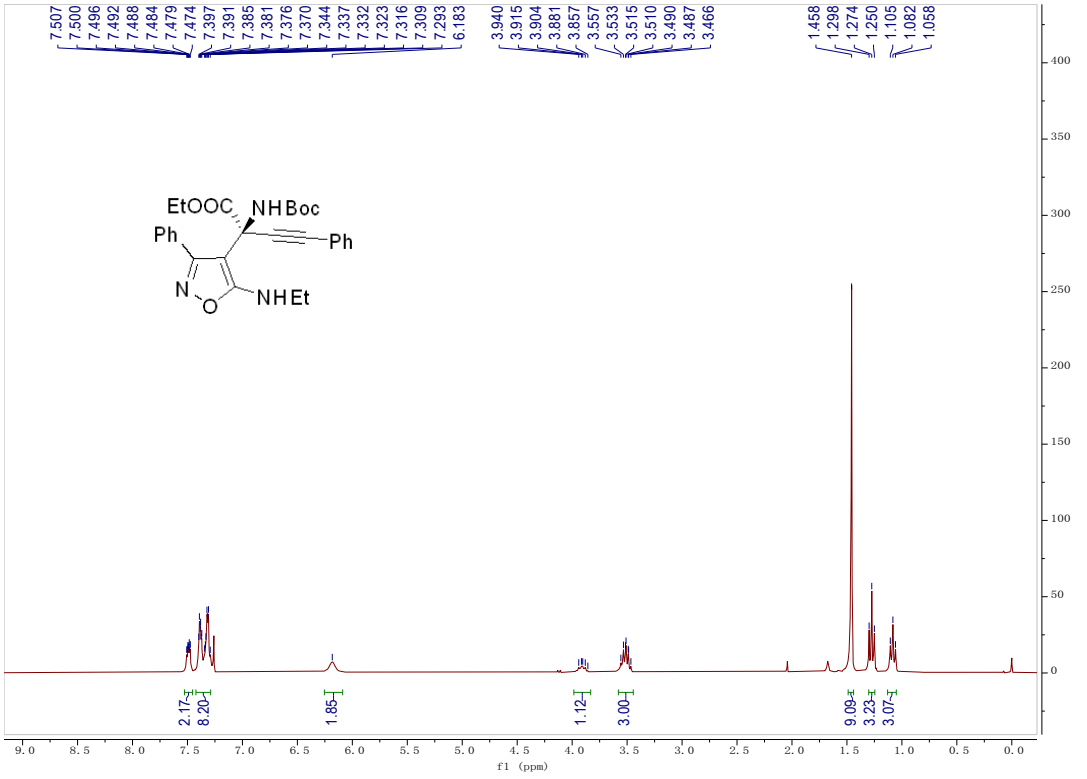
Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-(triisopropylsilyl)but-3-ynoate (2m)

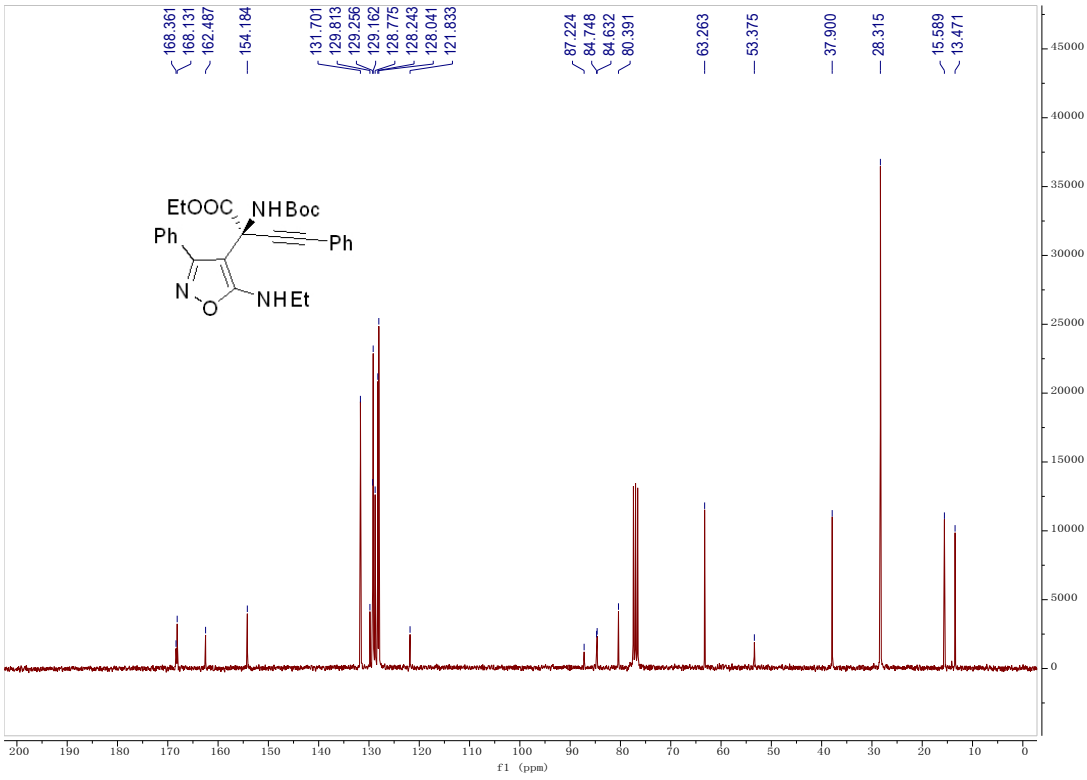


Ethyl (*E*)-2-((*tert*-butoxycarbonyl)imino)-4-cyclopropylbut-3-ynoate (2n)

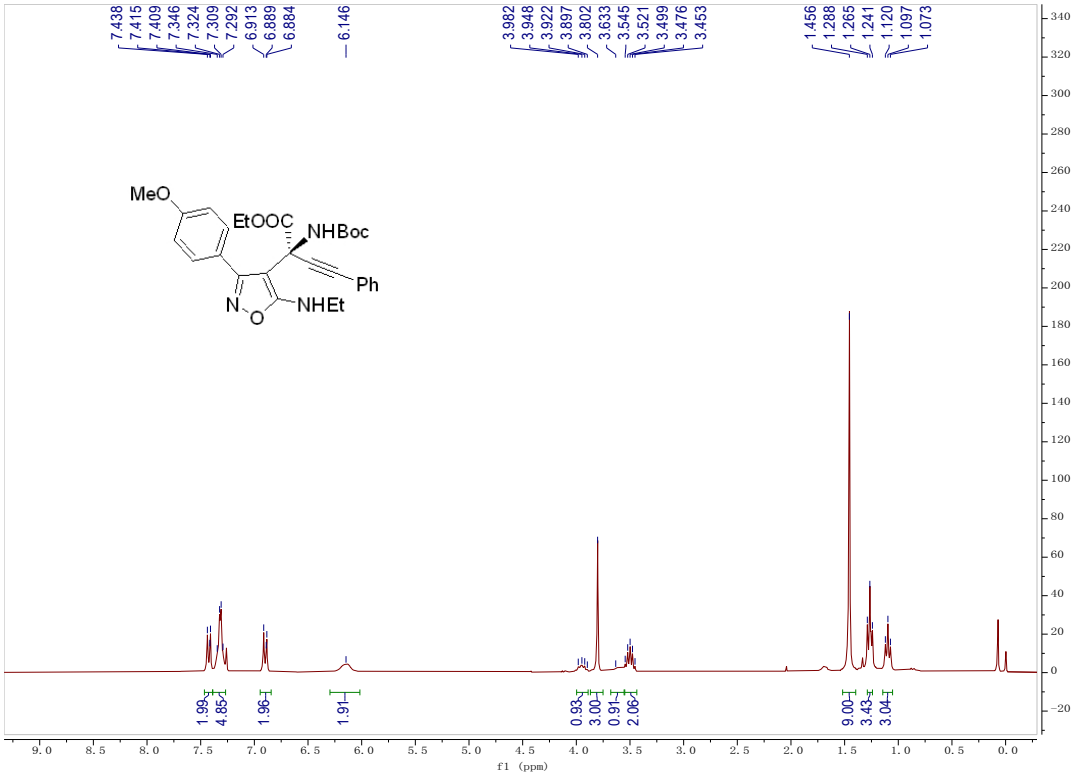


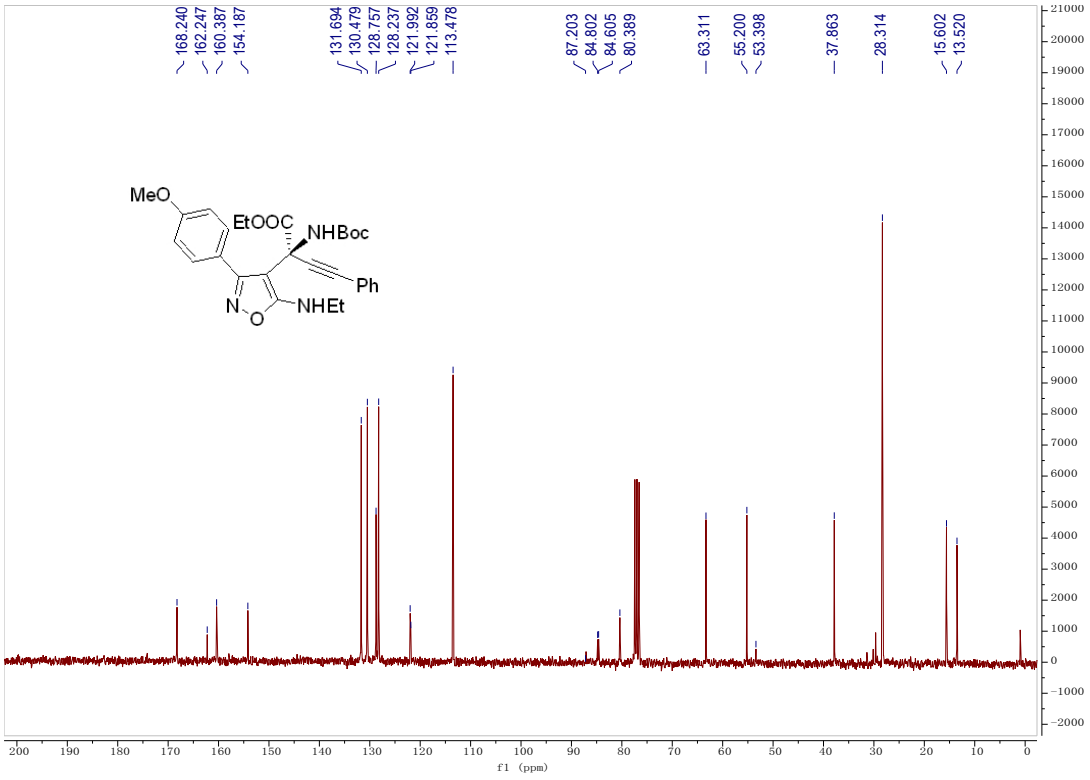
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3aa)



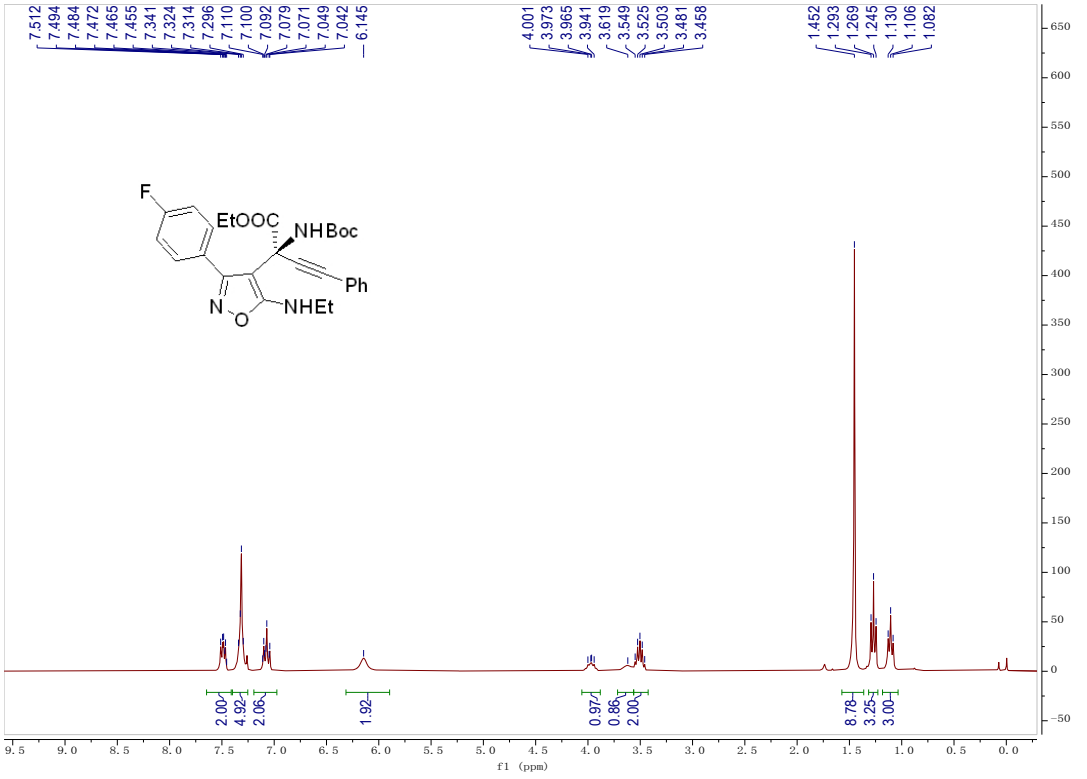


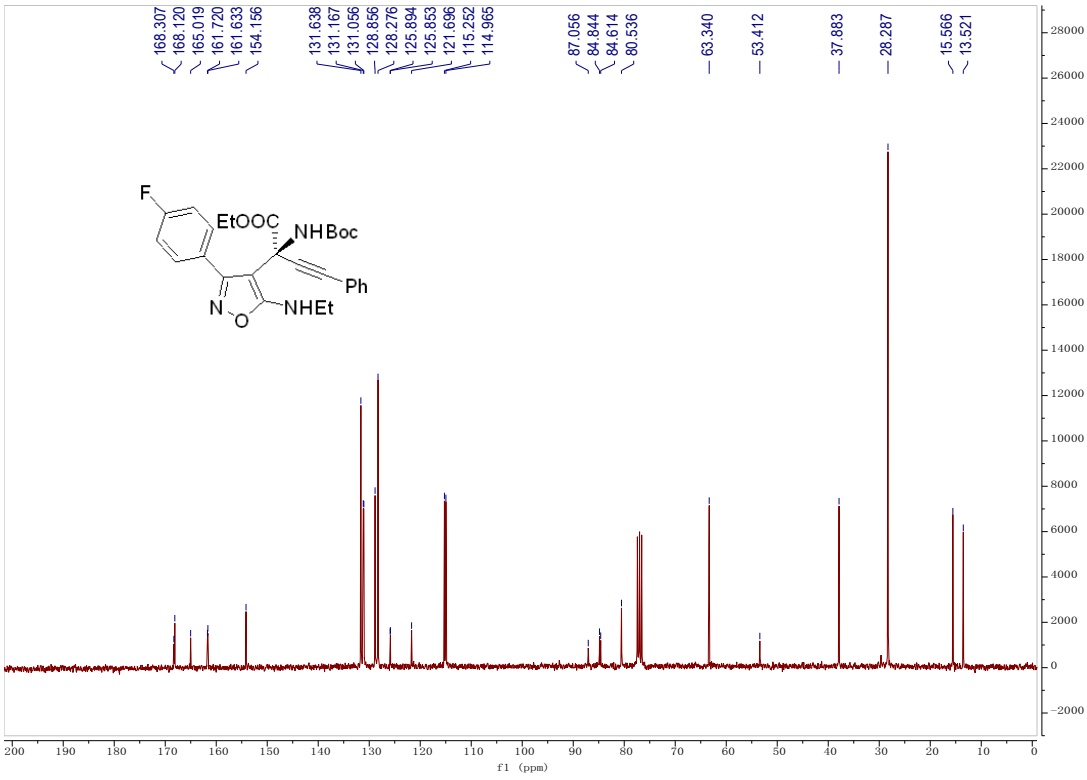
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ba)



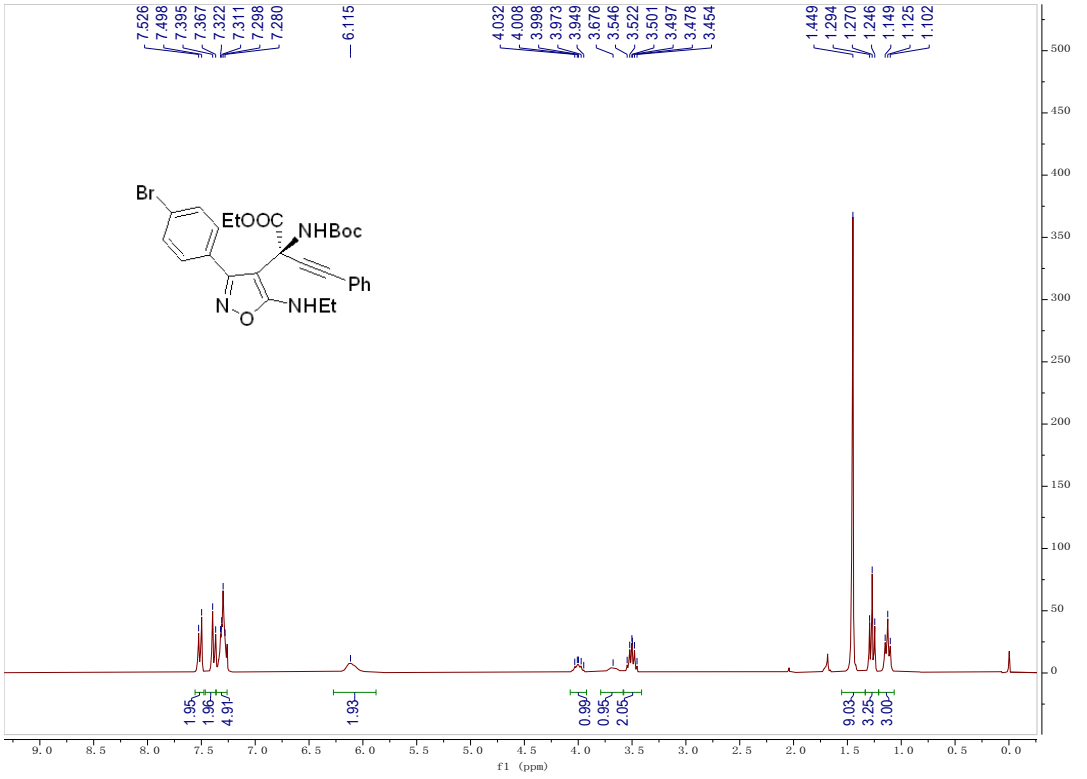


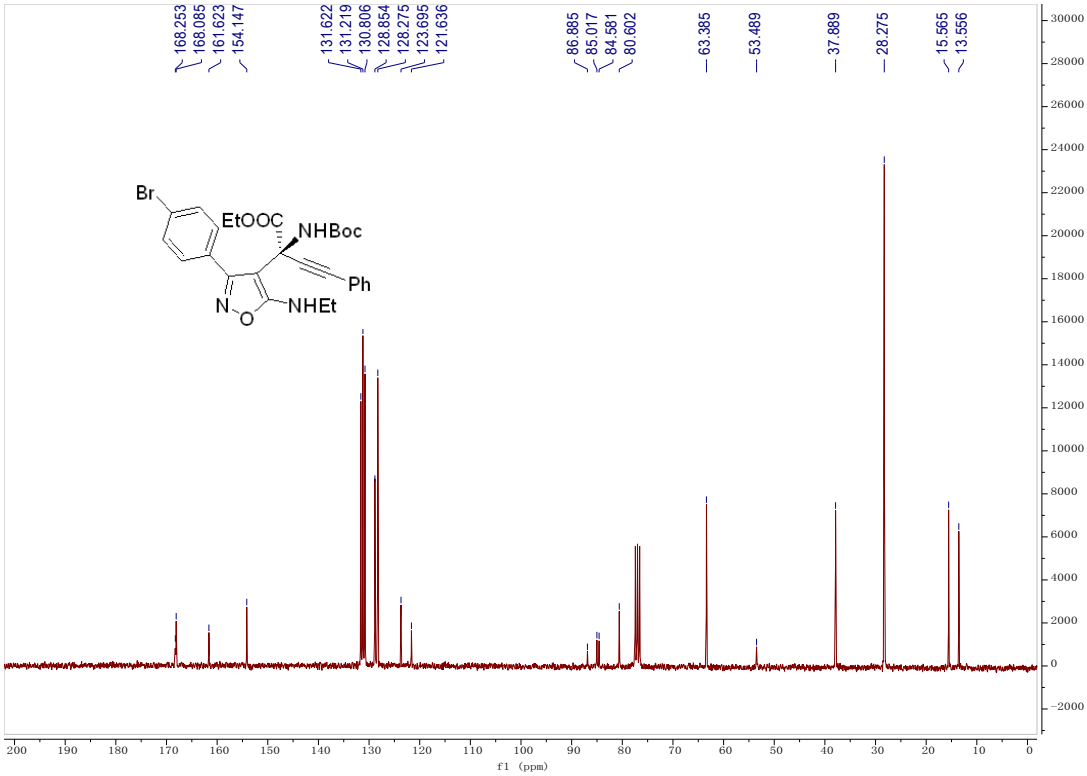
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-fluorophenyl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ca)



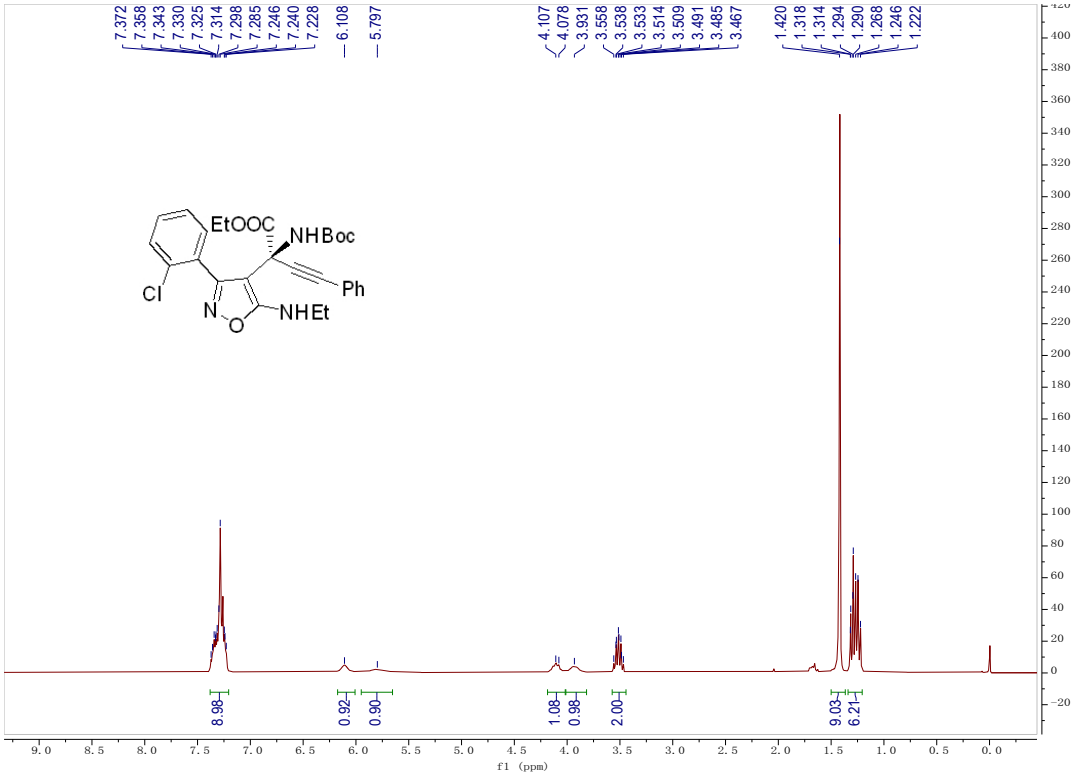


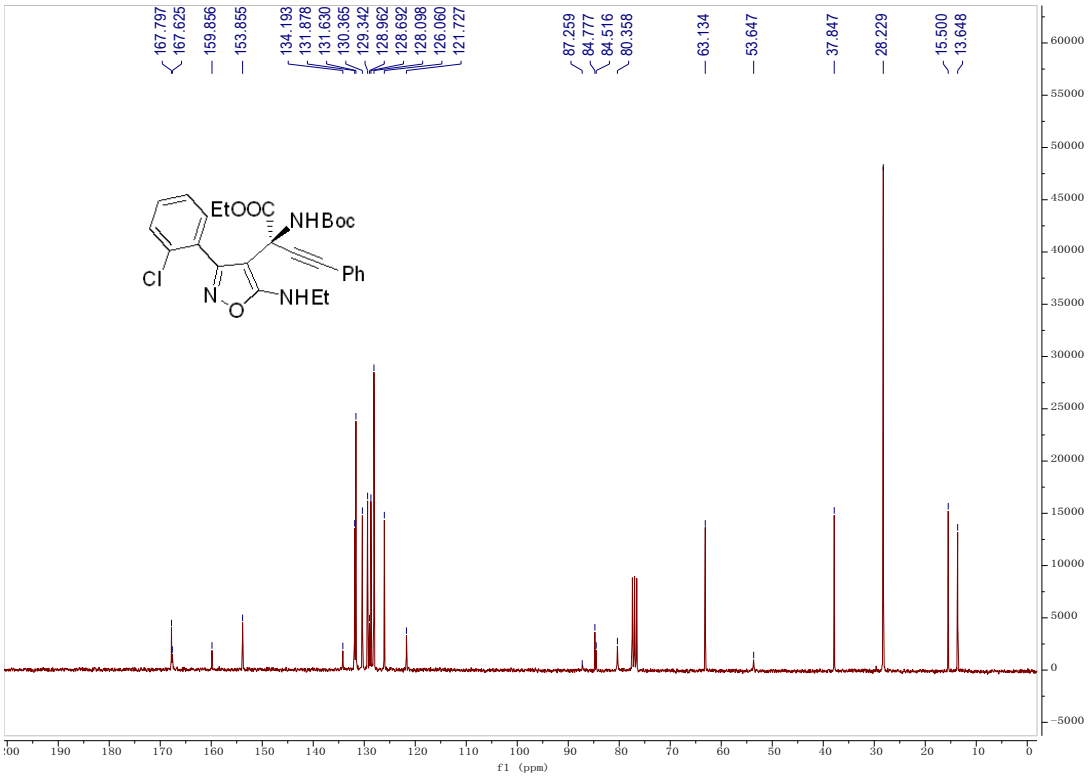
Ethyl (*S*)-2-(3-(4-bromophenyl)-5-(ethylamino)isoxazol-4-yl)-2-((*tert*-butoxycarbonyl)amino)-4-phenylbut-3-ynoate (3da)



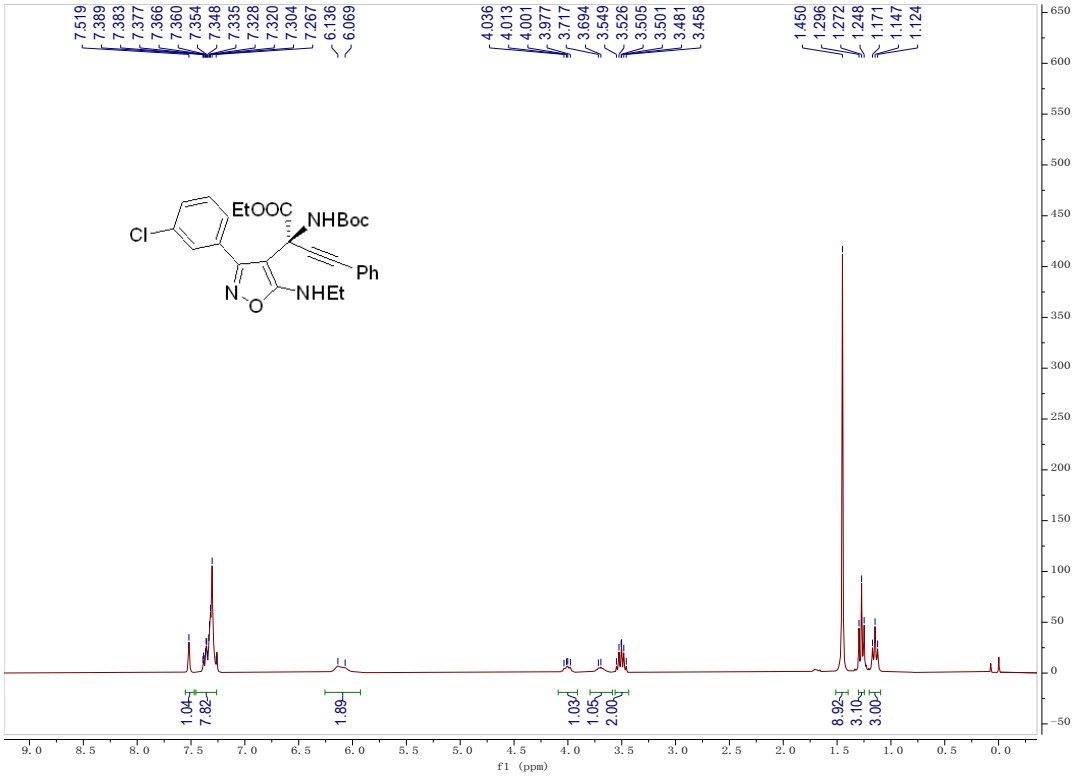


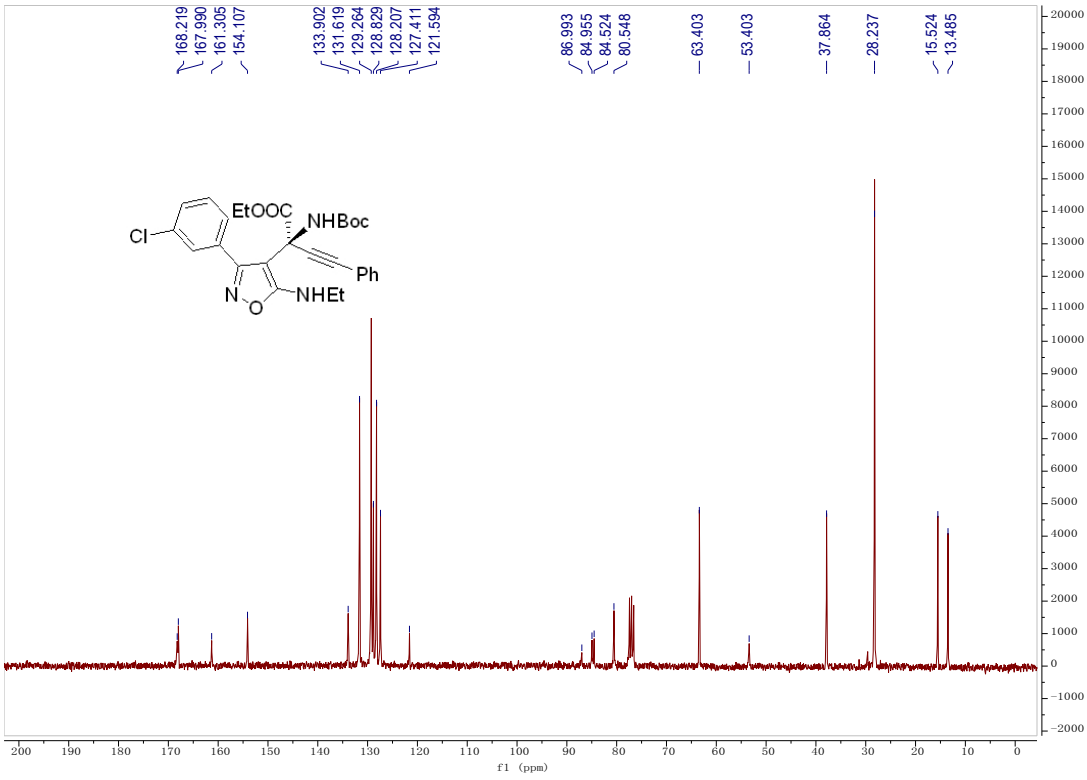
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(2-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ea)



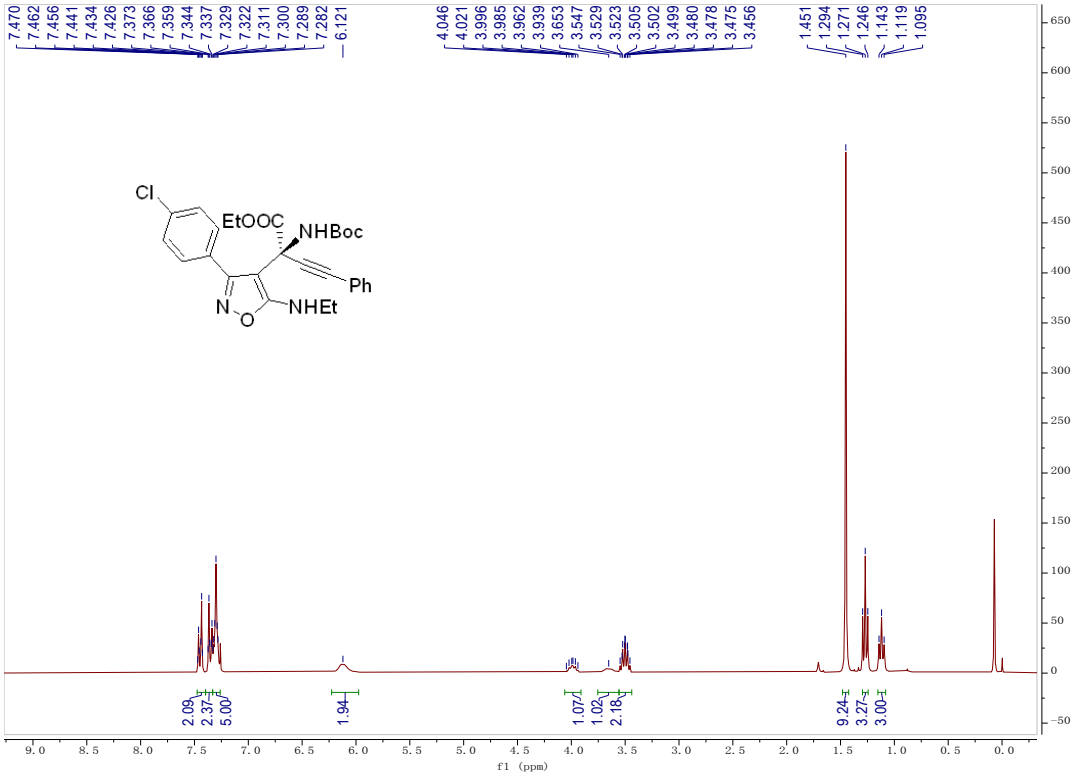


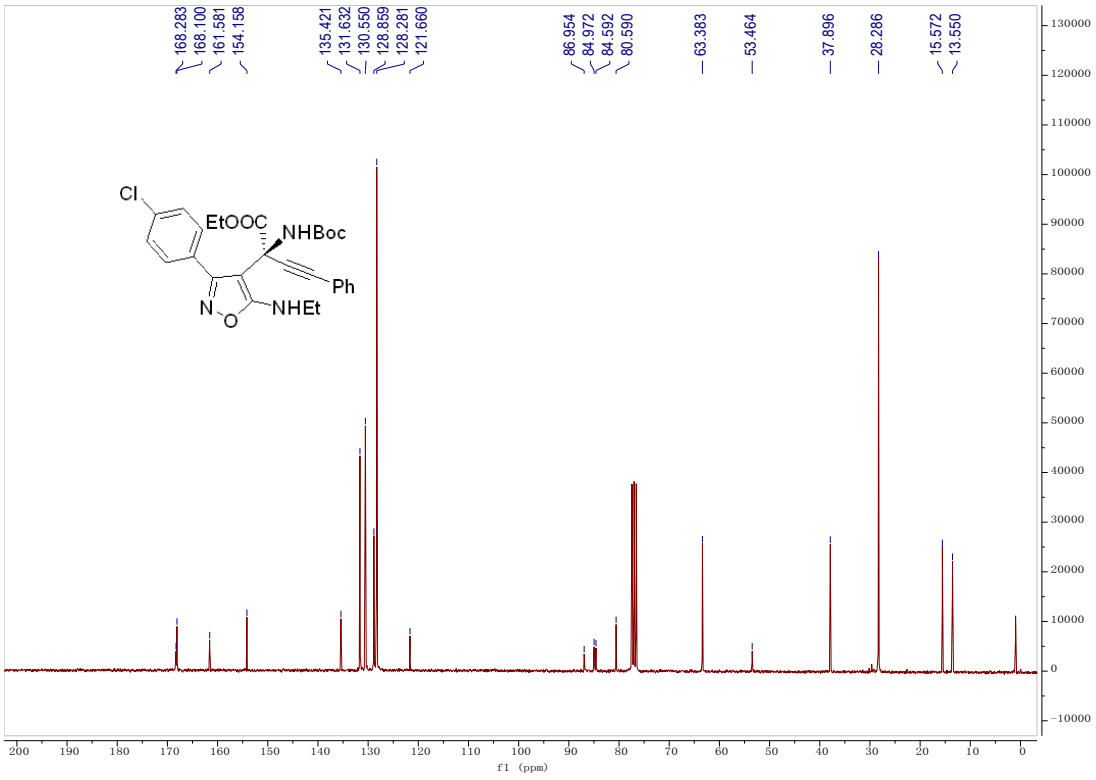
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(3-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3fa)



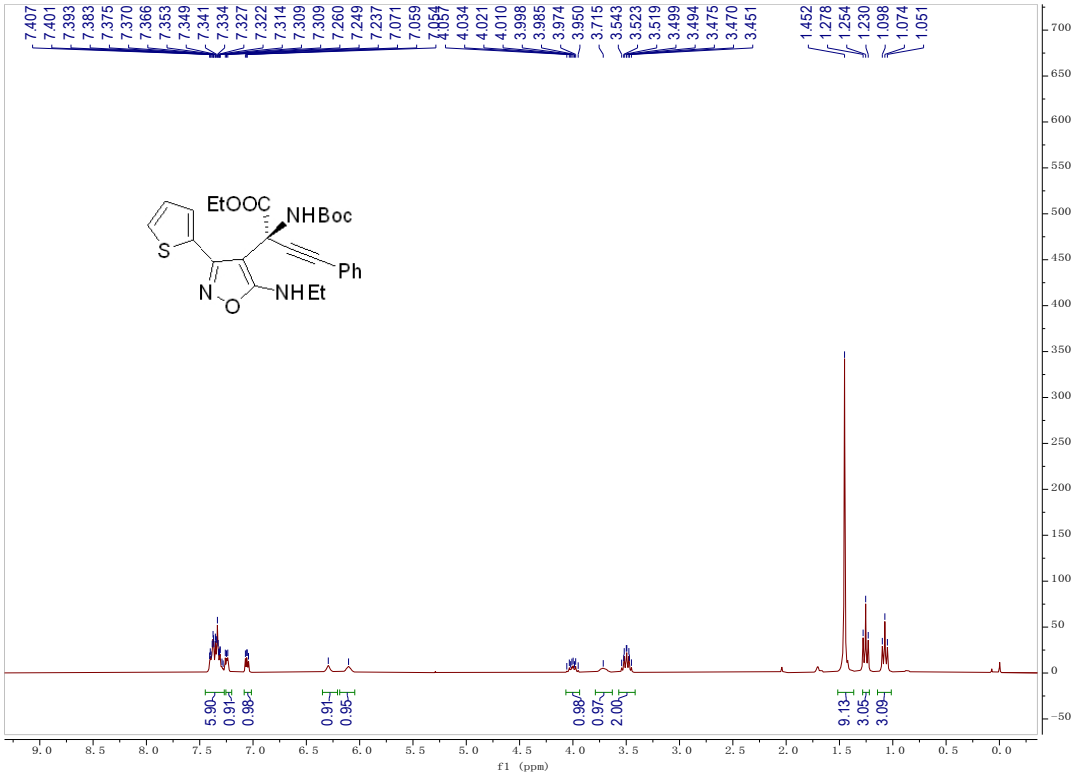


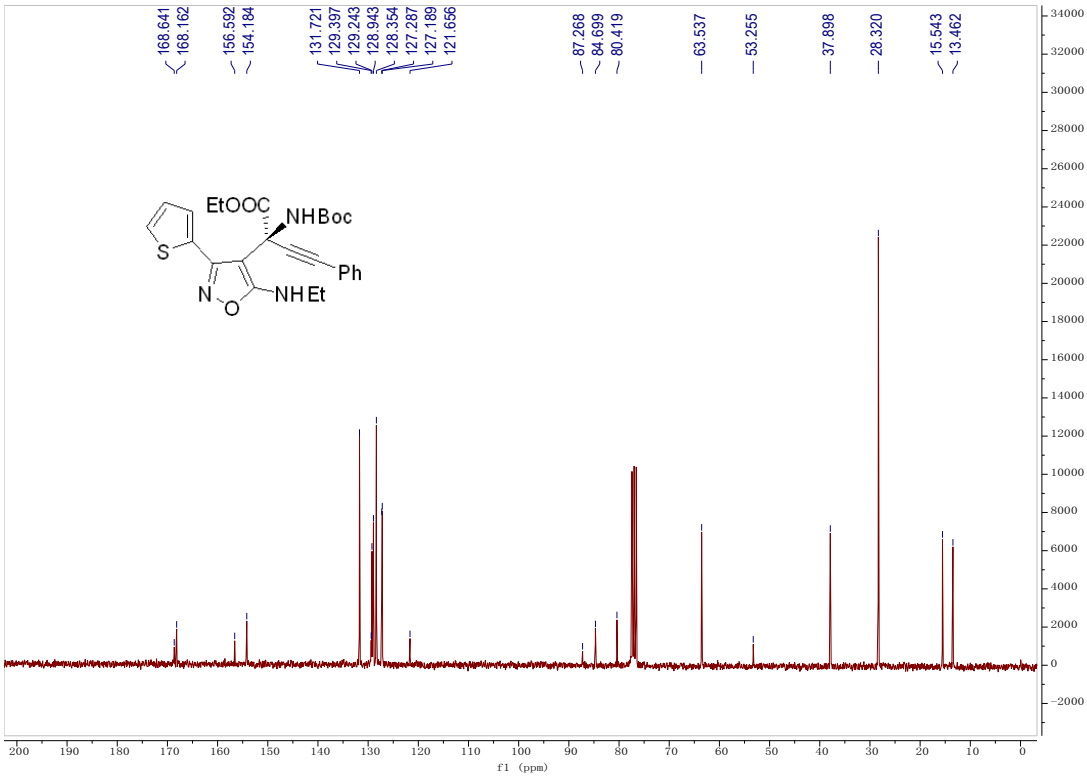
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(4-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ga)



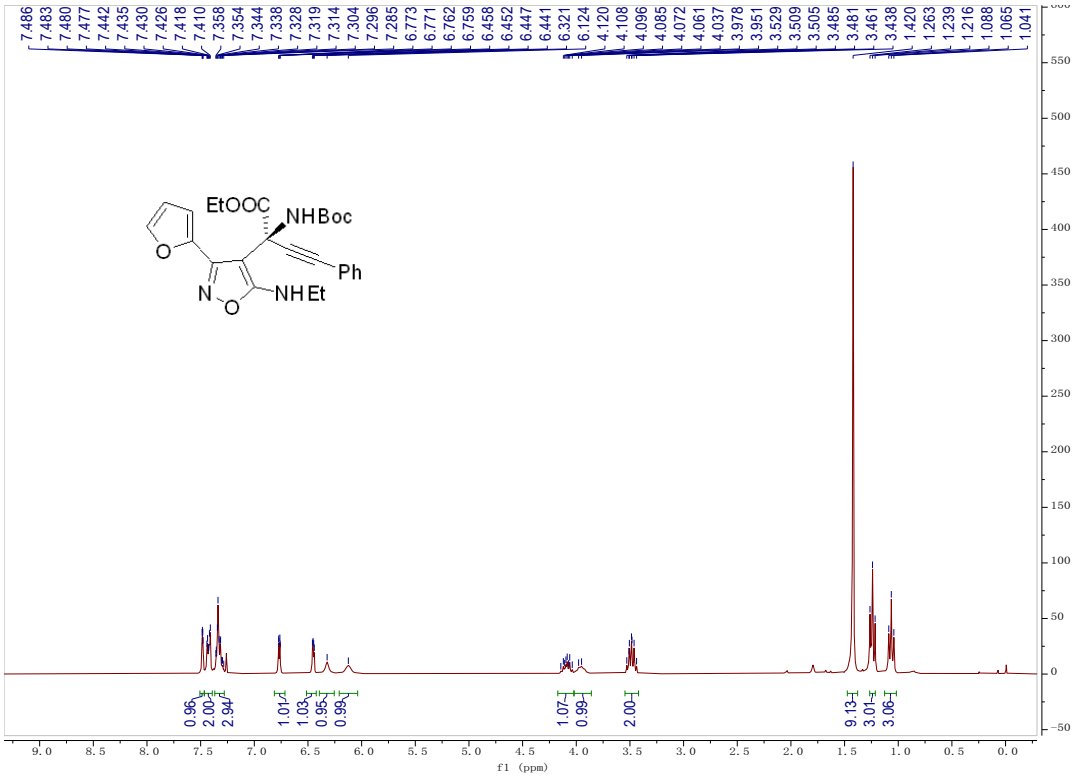


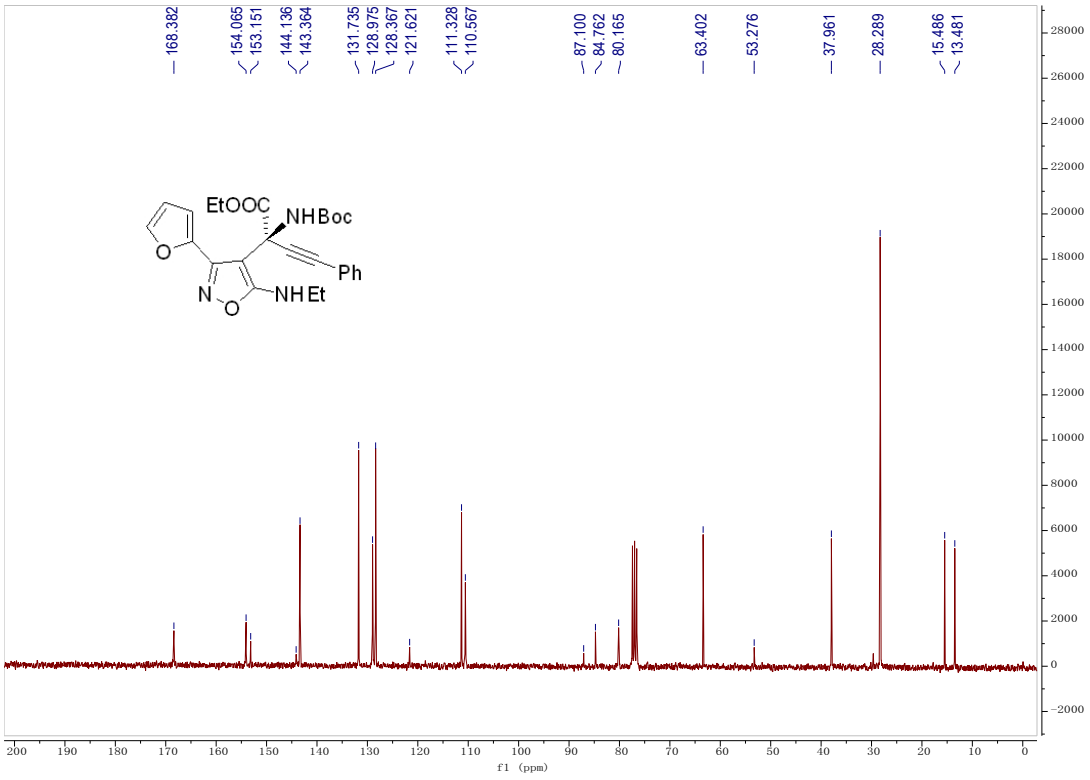
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(thiophen-2-yl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ha)



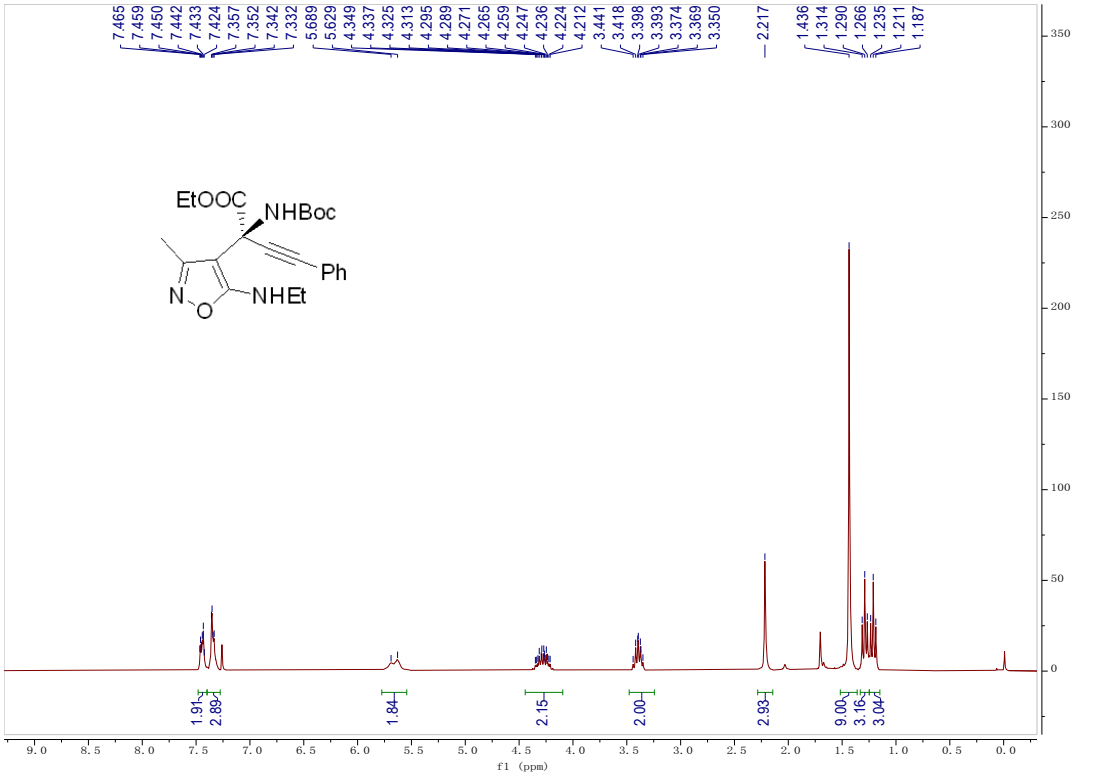


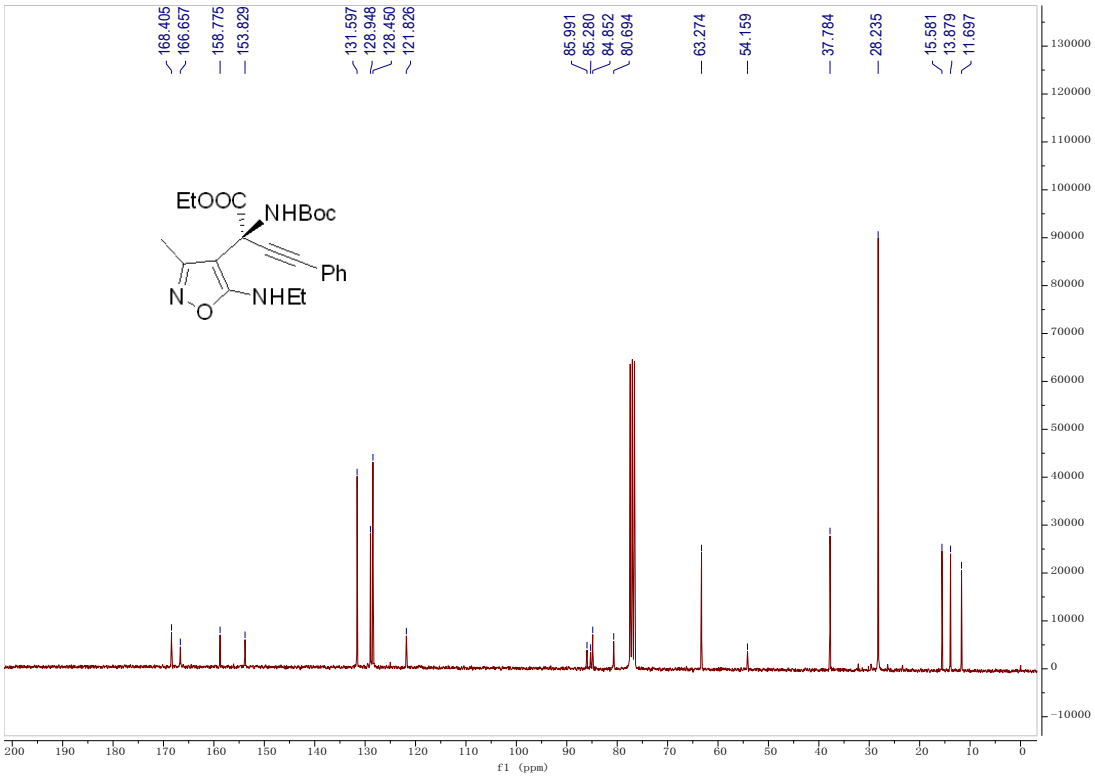
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(furan-2-yl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ia)



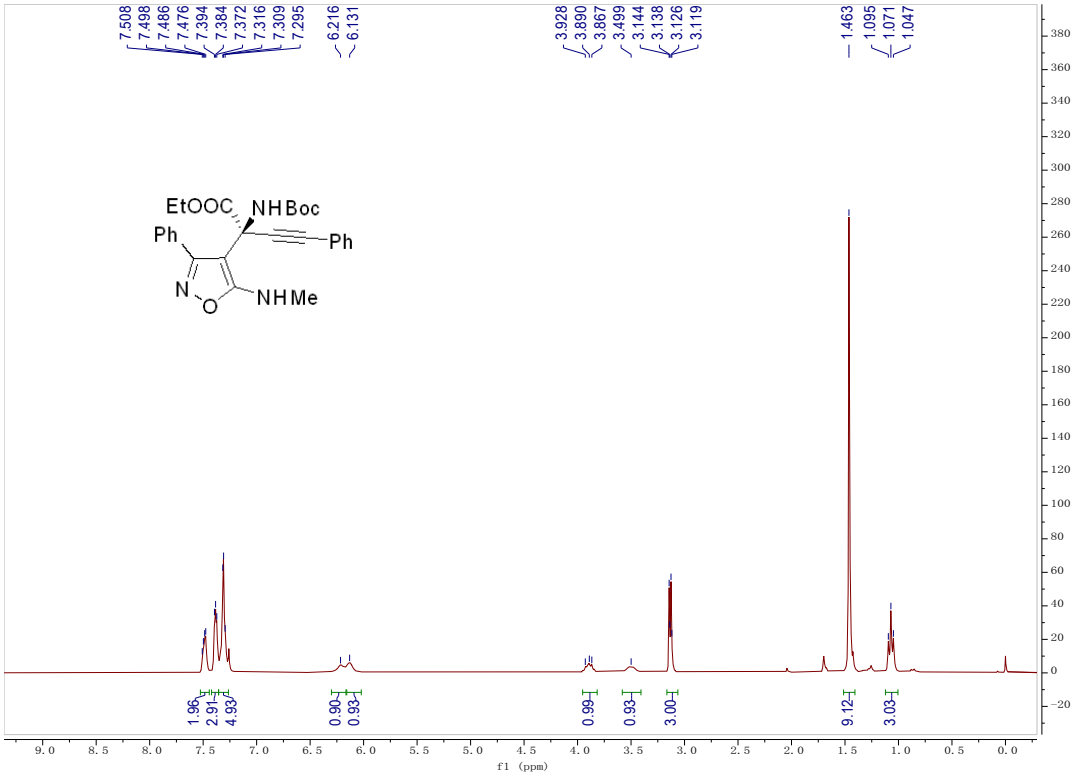


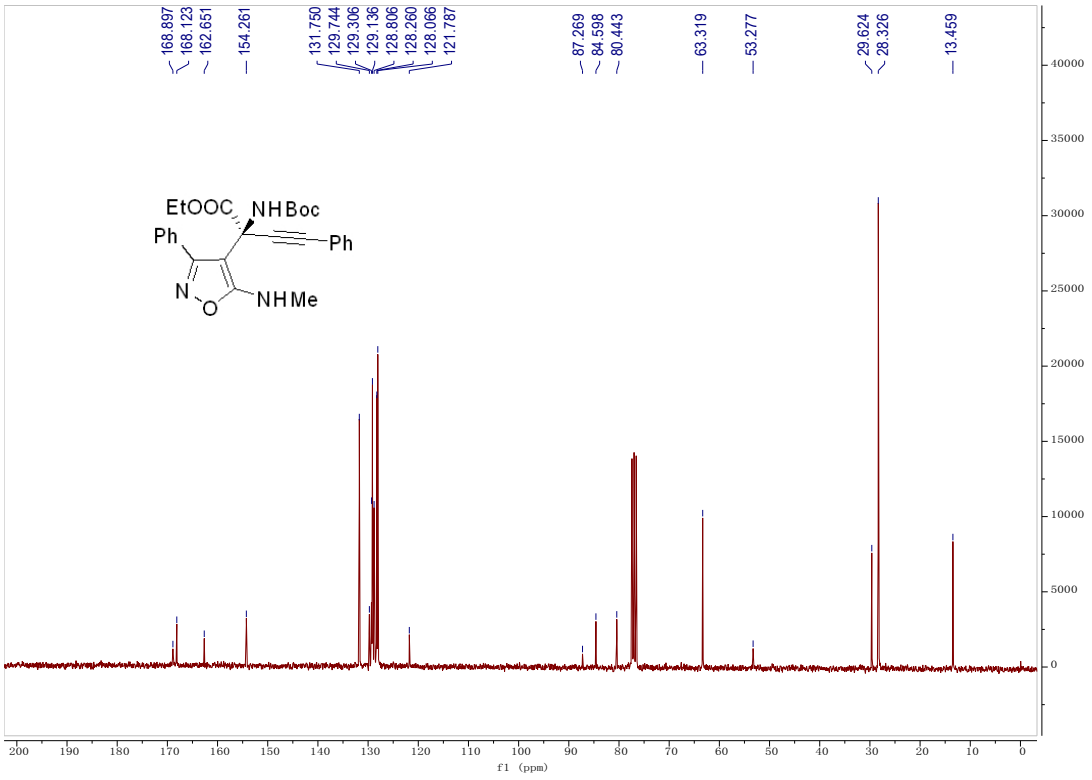
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-methylisoxazol-4-yl)-4-phenylbut-3-ynoate (3ja)



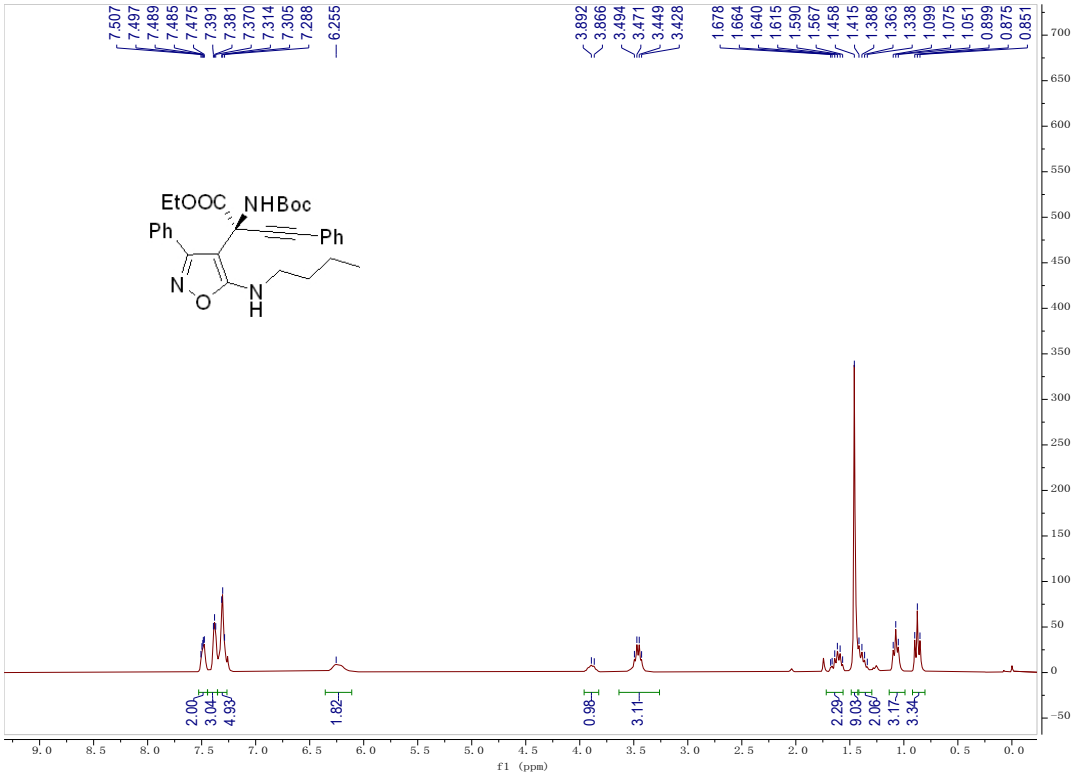


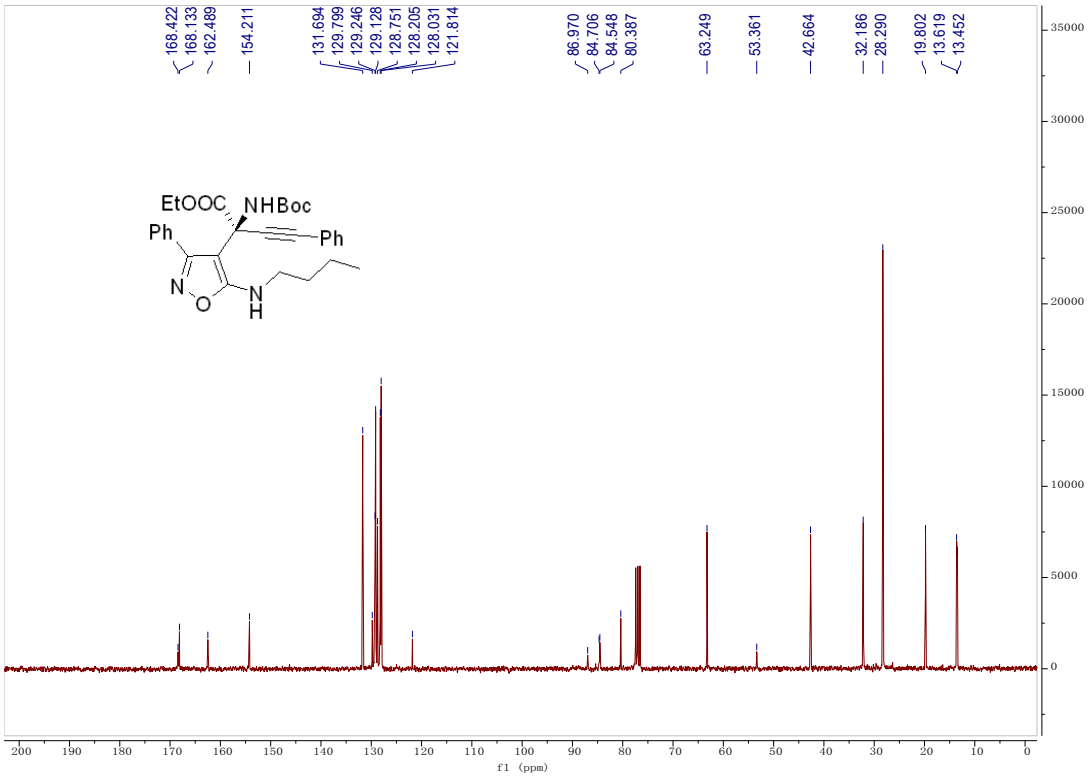
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(methylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3la)



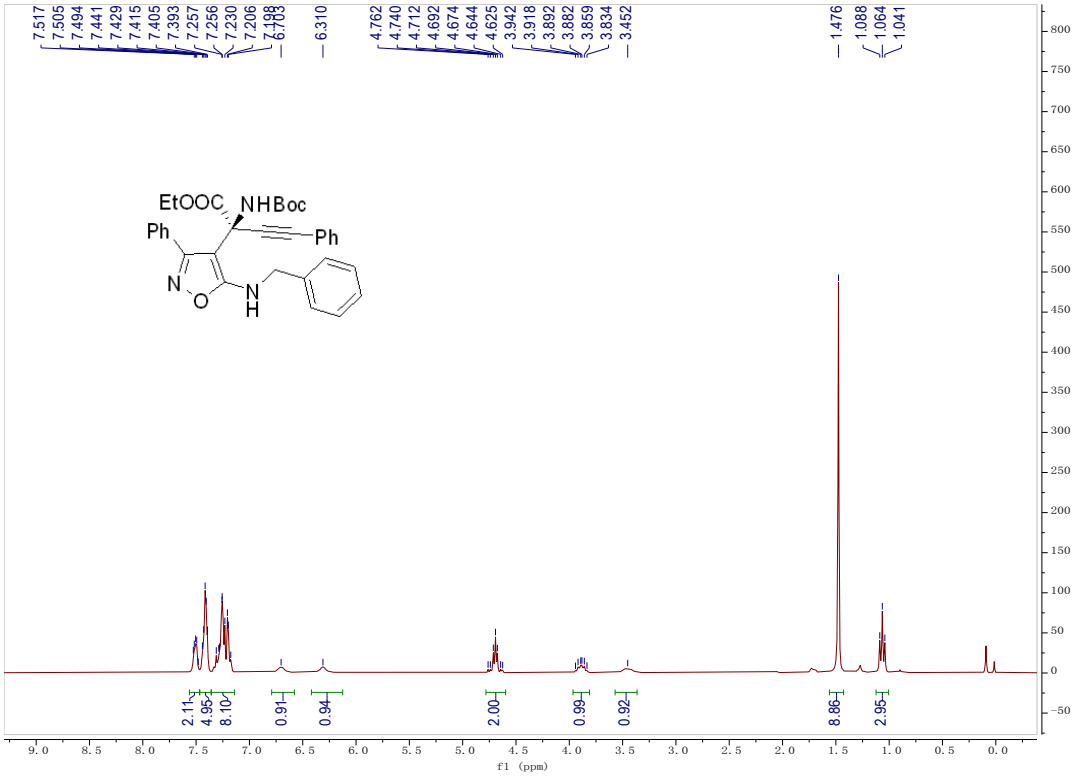


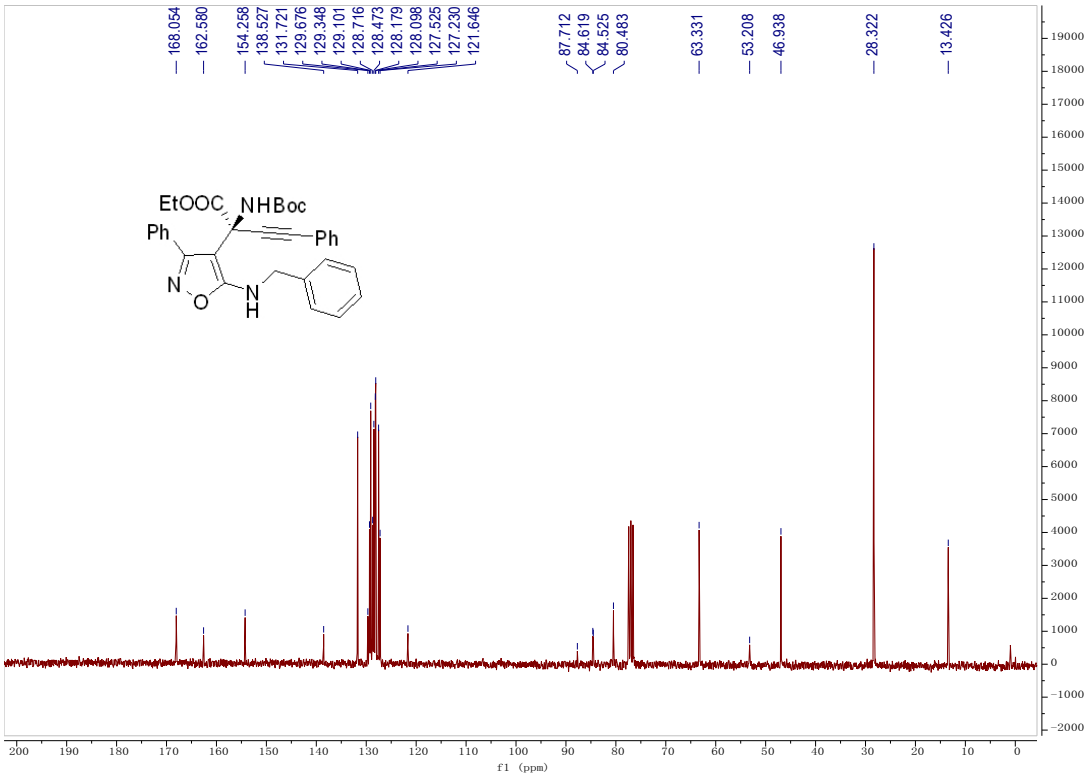
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(butylamino)-3-phenylisoxazol-4-yl)-4-phenylbut-3-ynoate (3ma)



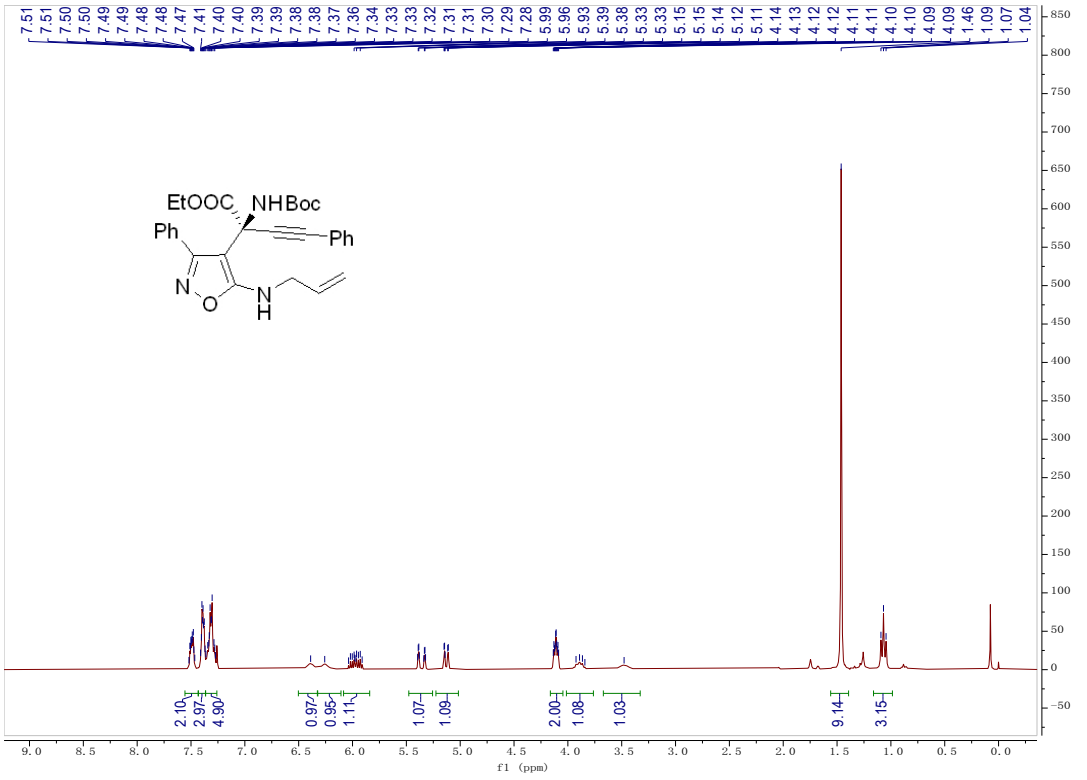


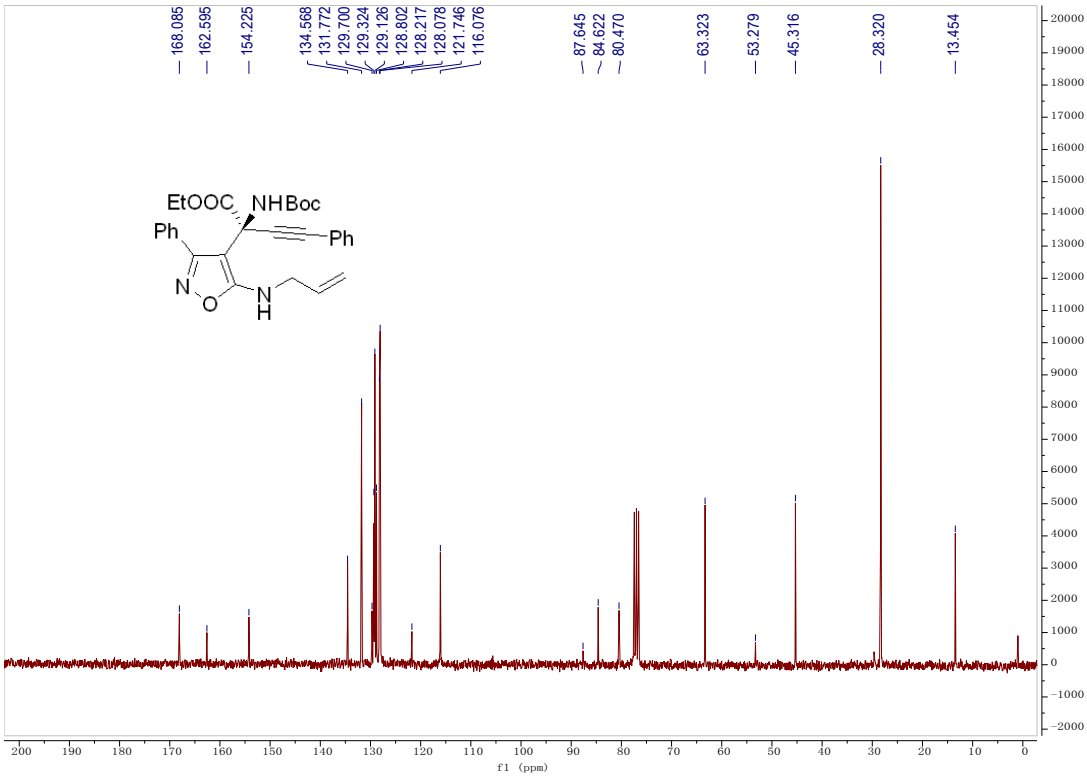
Ethyl (*S*)-2-(5-(benzylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl) amino)-4-phenylbut-3-ynoate (3na)



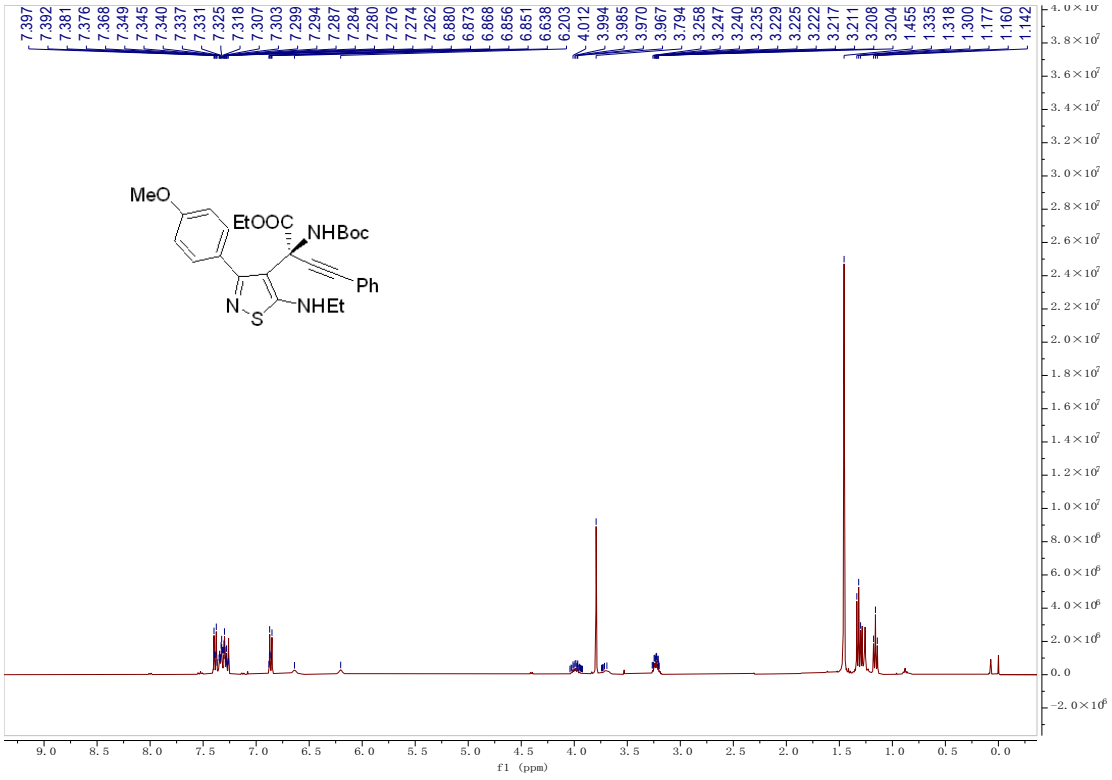


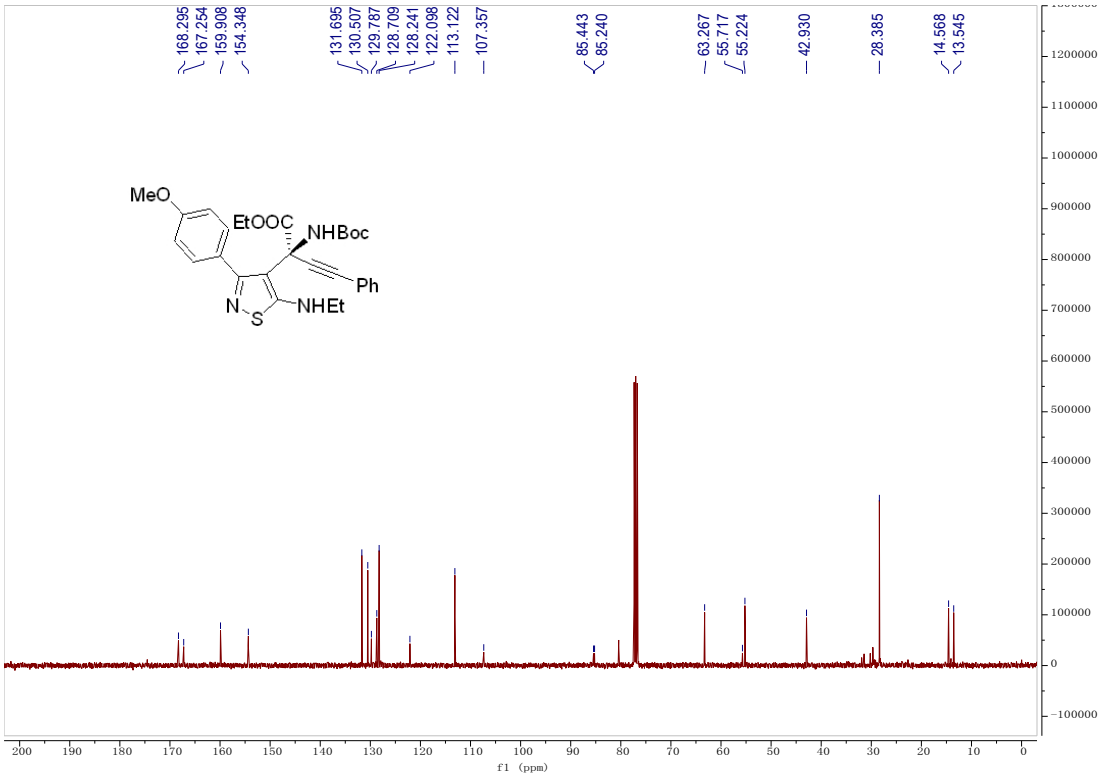
Ethyl (*S*)-2-(5-(allylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl) amino)-4-phenylbut-3-ynoate (3oa)



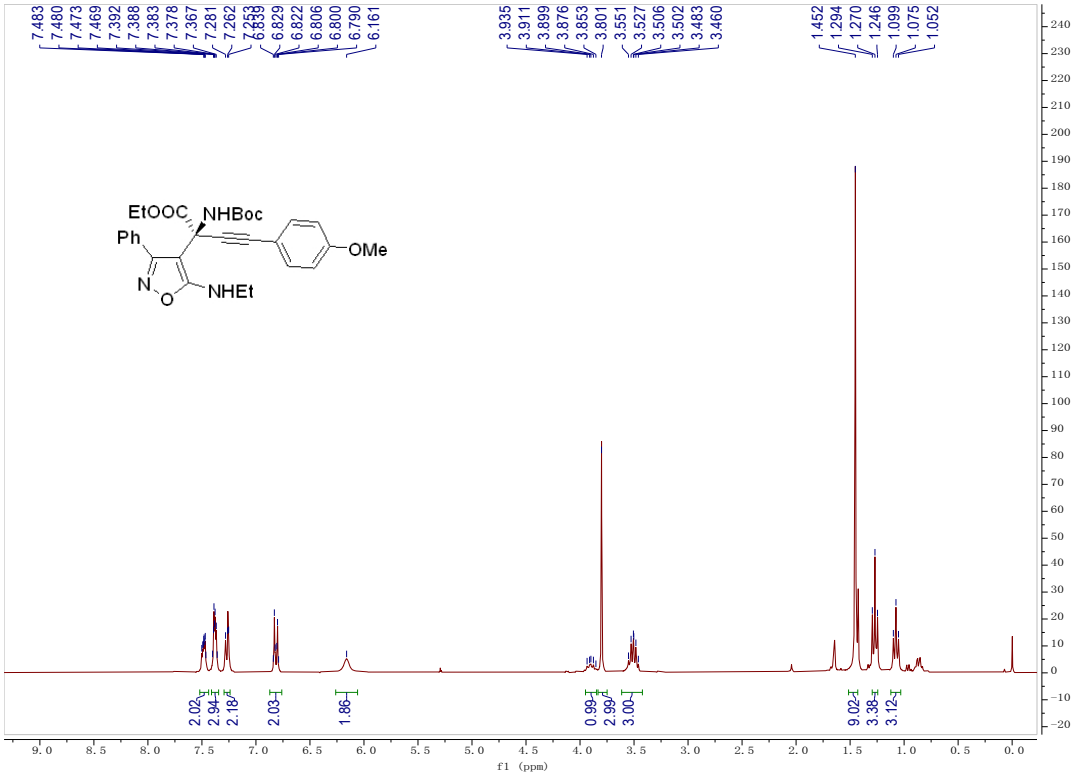


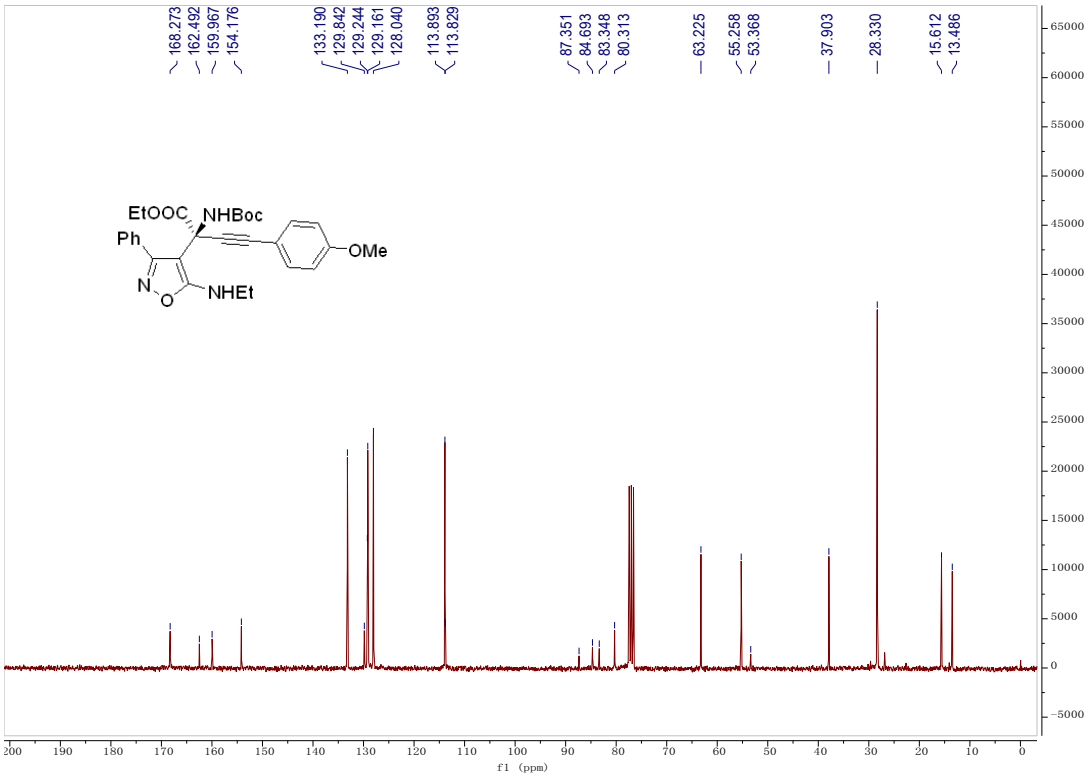
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl) isothiazol-4-yl)-4-phenylbut-3-ynoate (3qa)



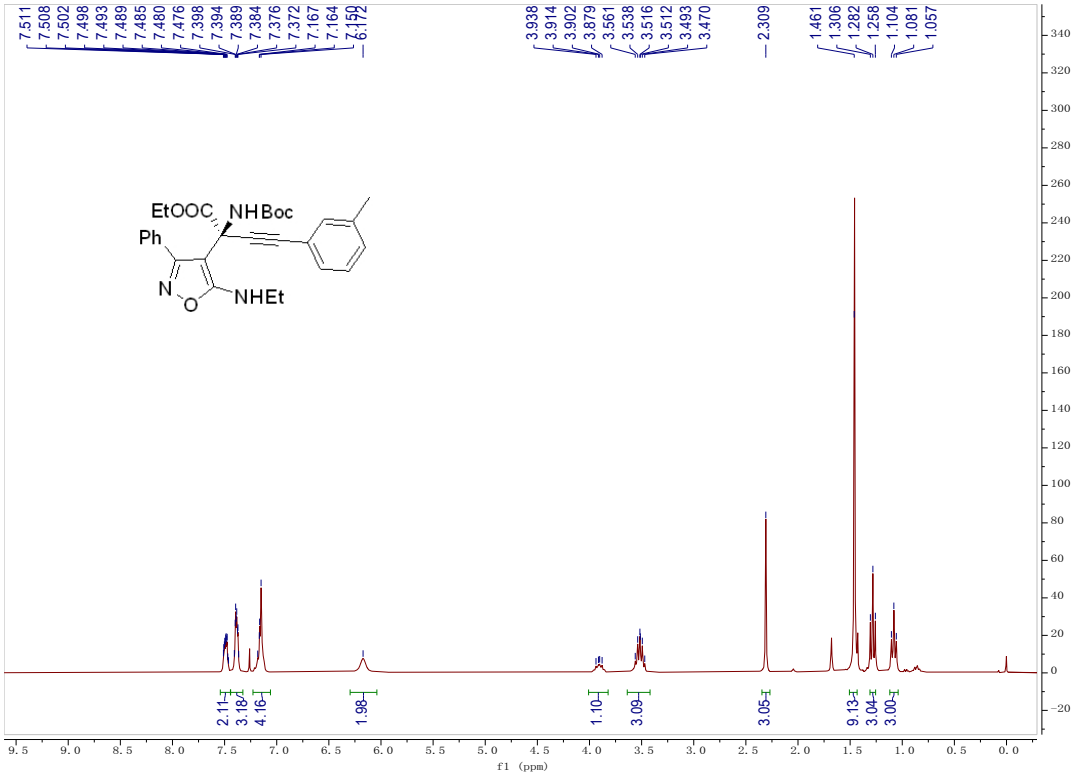


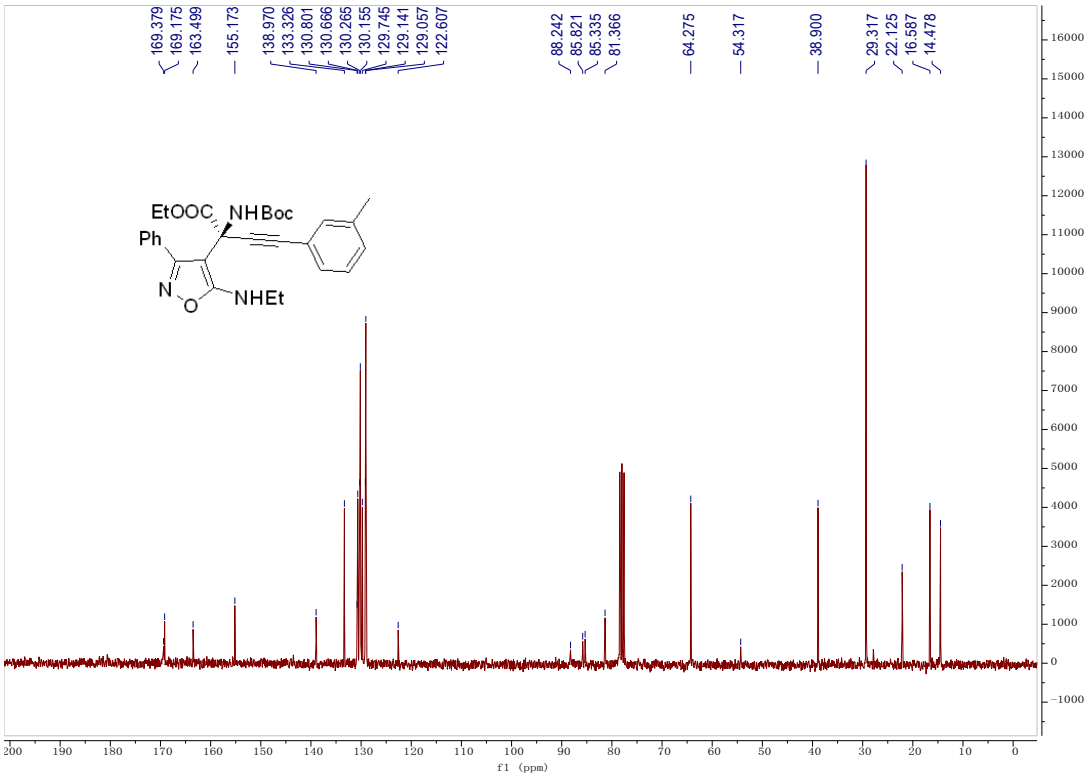
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-methoxyphenyl)but-3-ynoate (3ab)



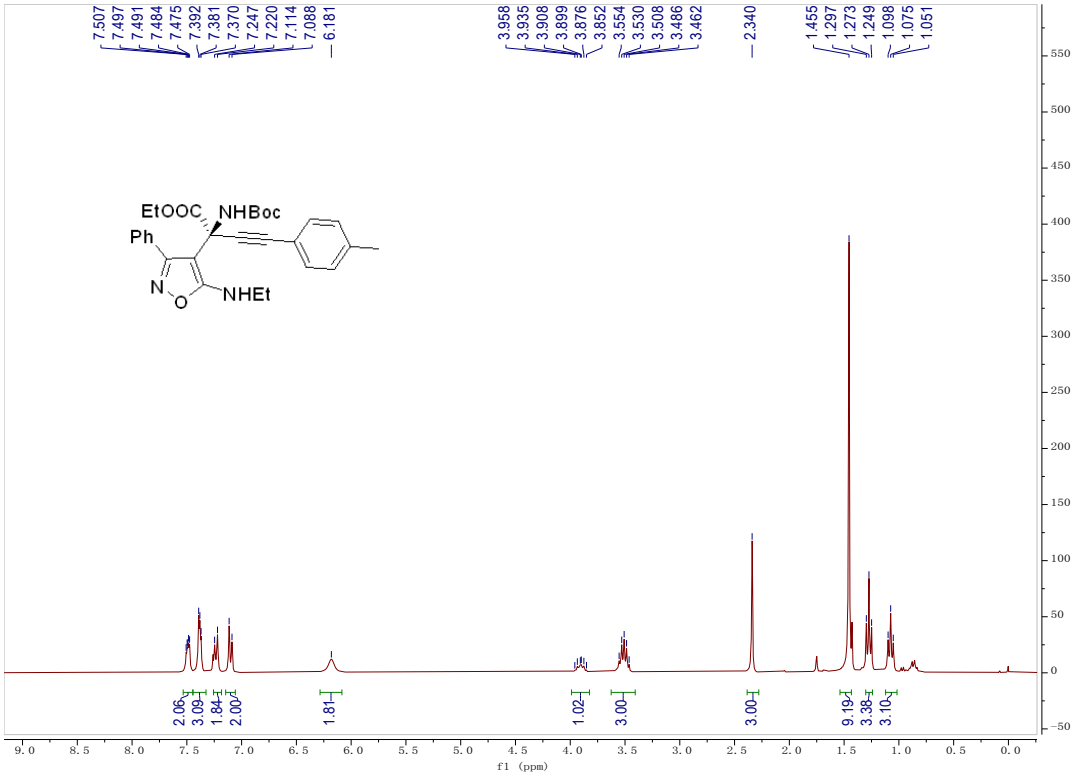


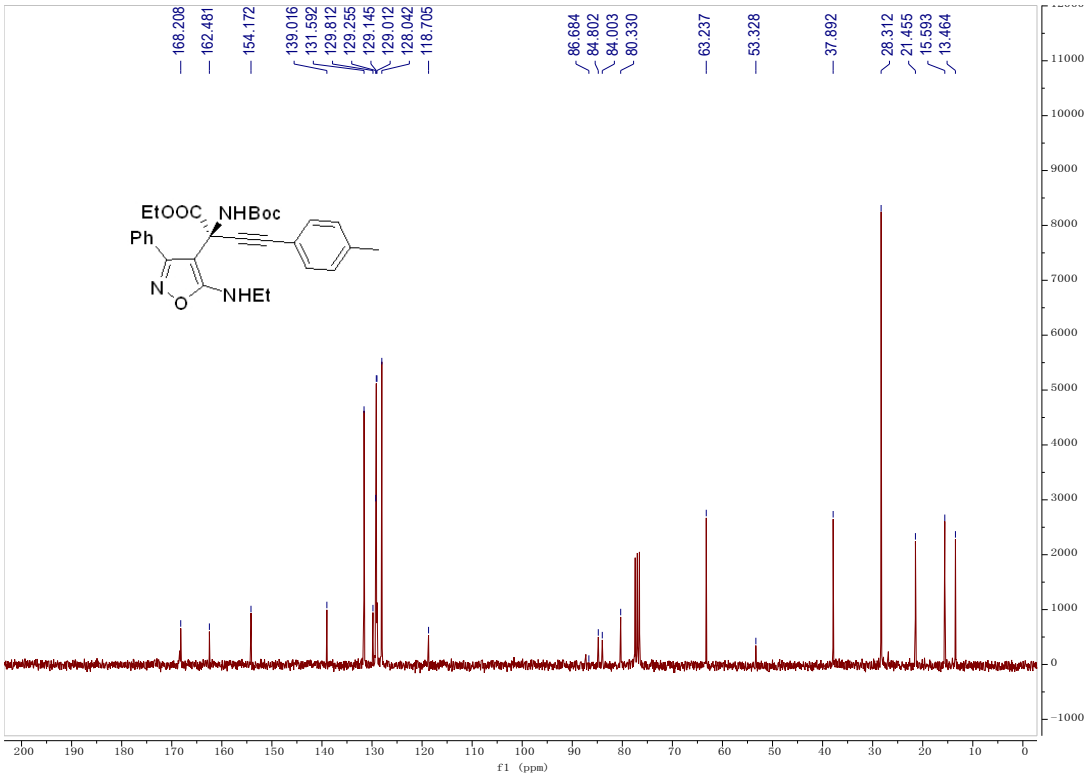
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(m-tolyl)but-3-ynoate (3ac)



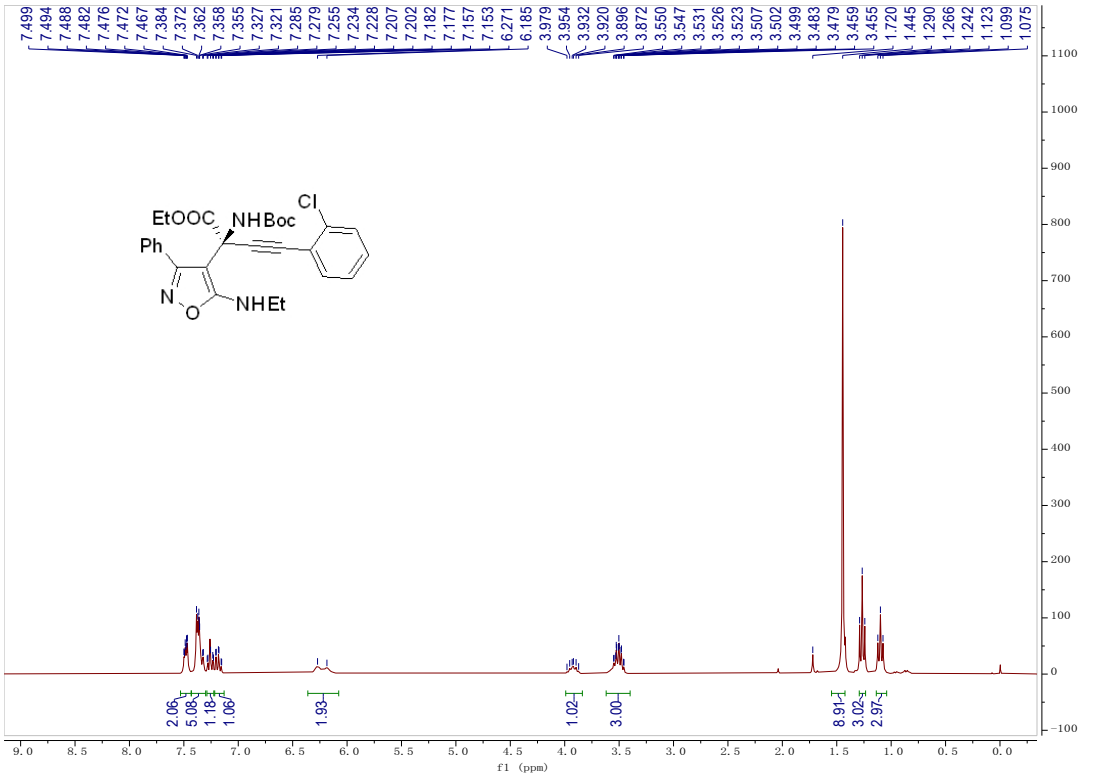


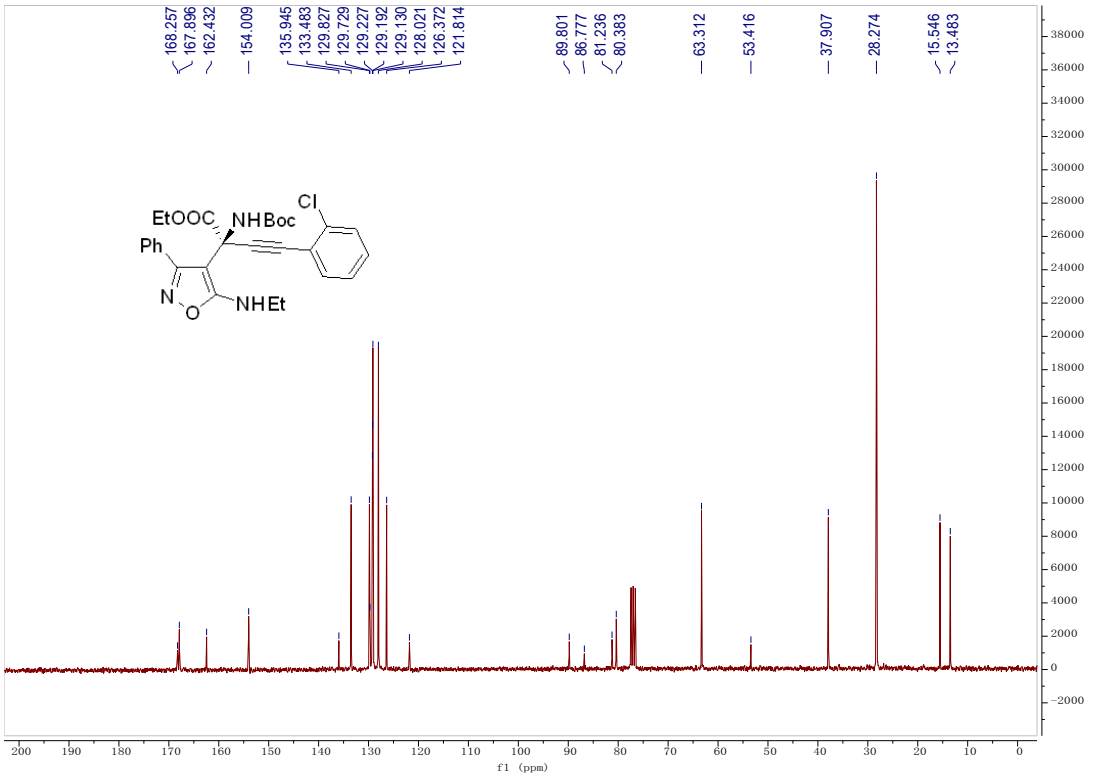
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(p-tolyl)but-3-ynoate (3ad)



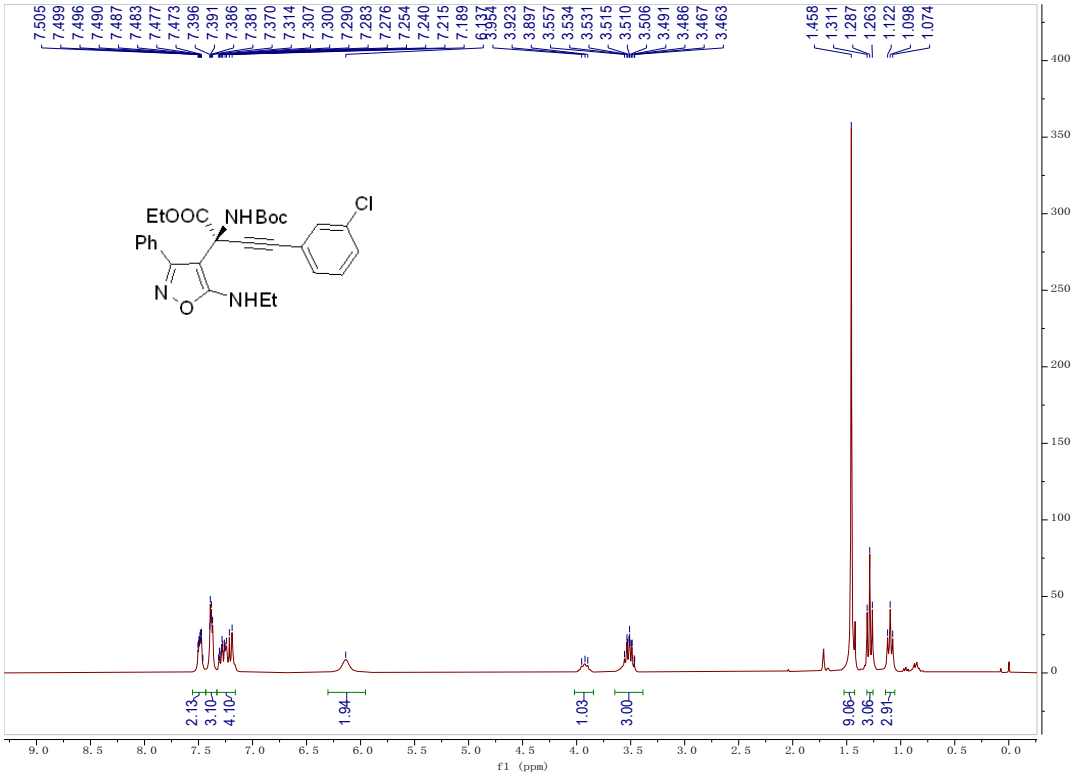


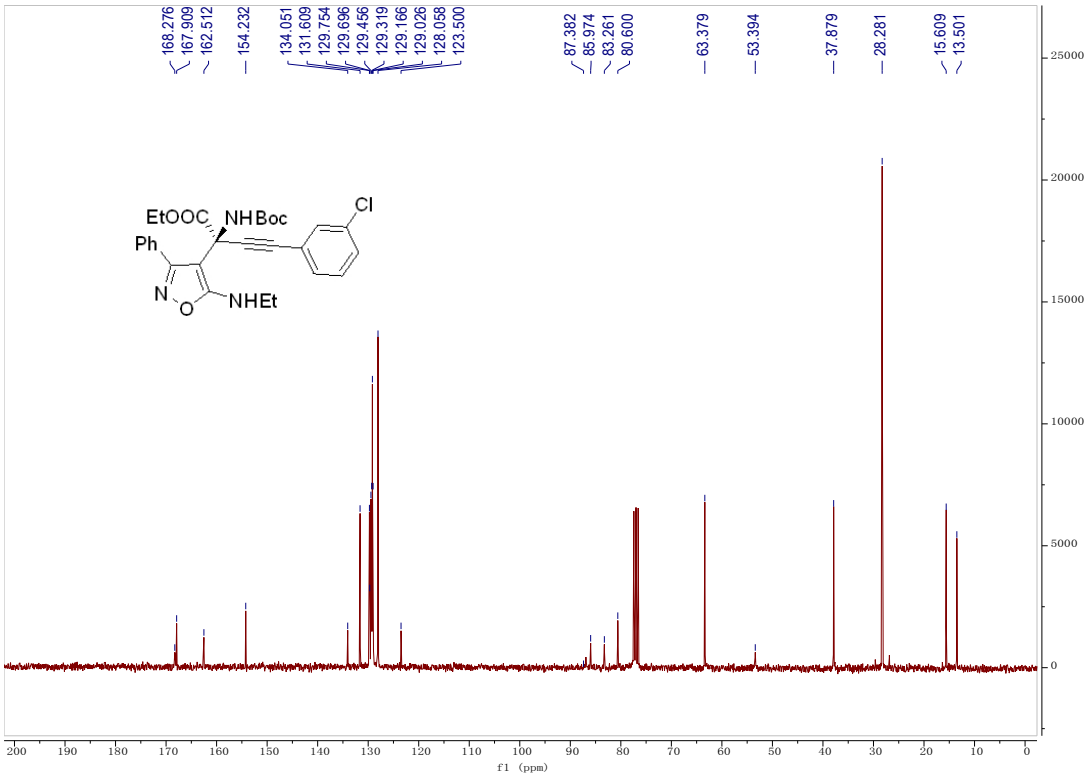
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(2-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ae)



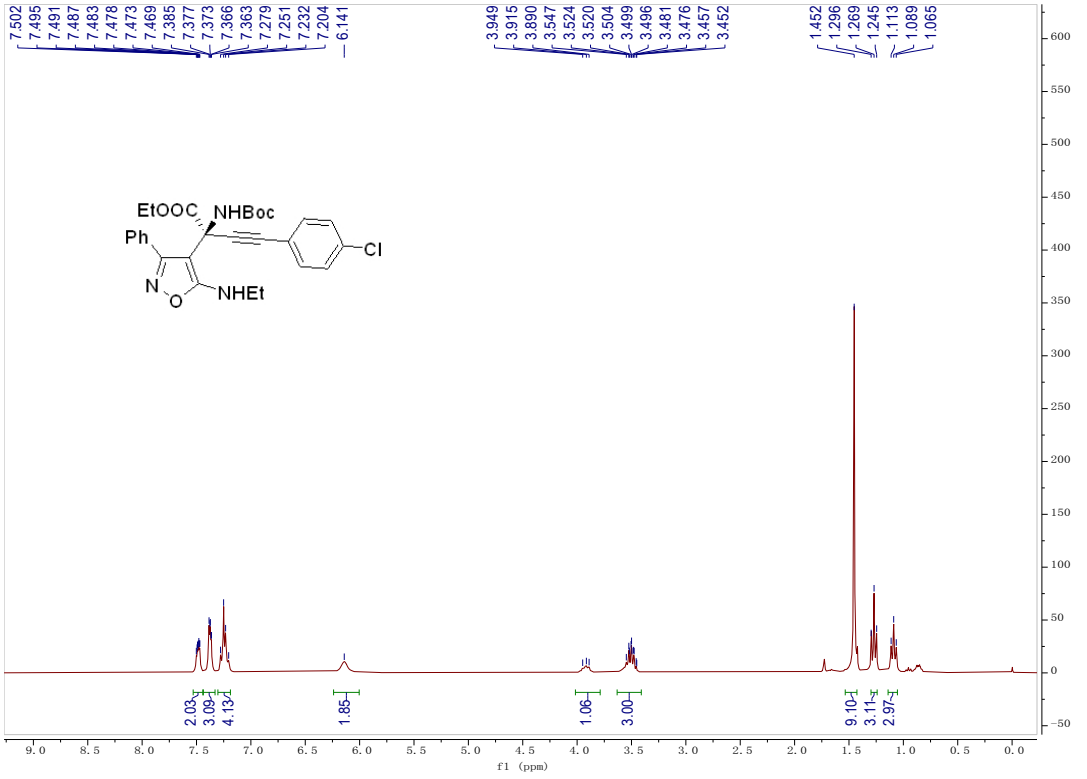


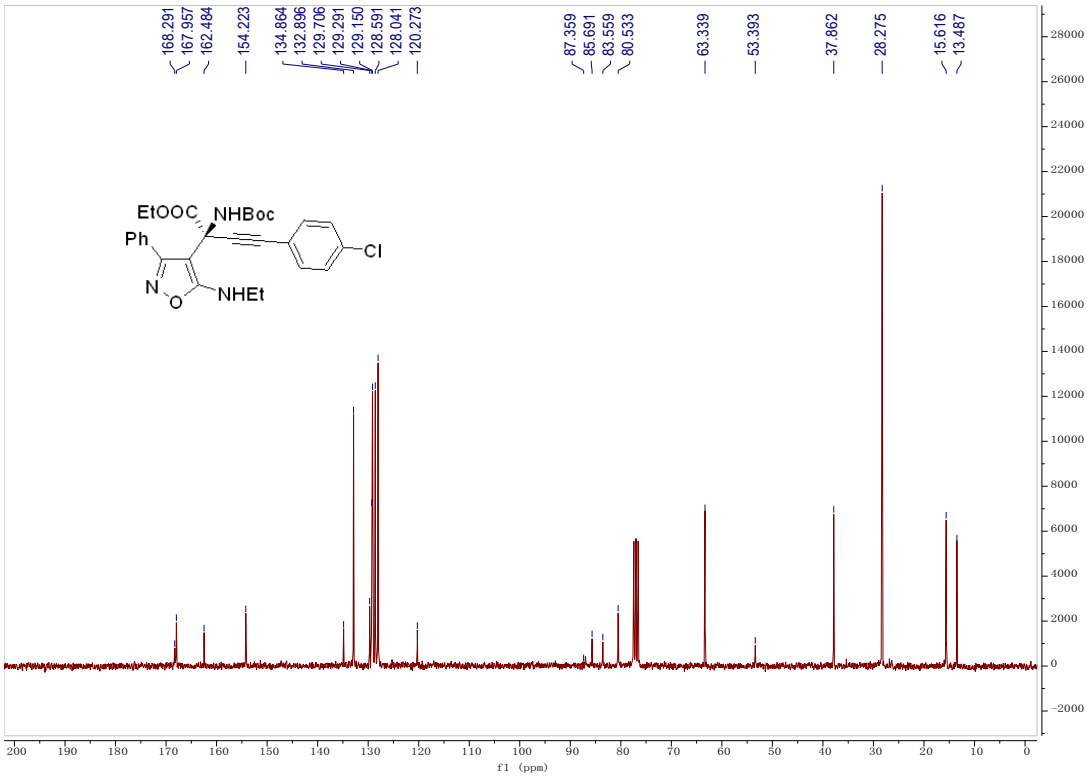
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(3-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3af)



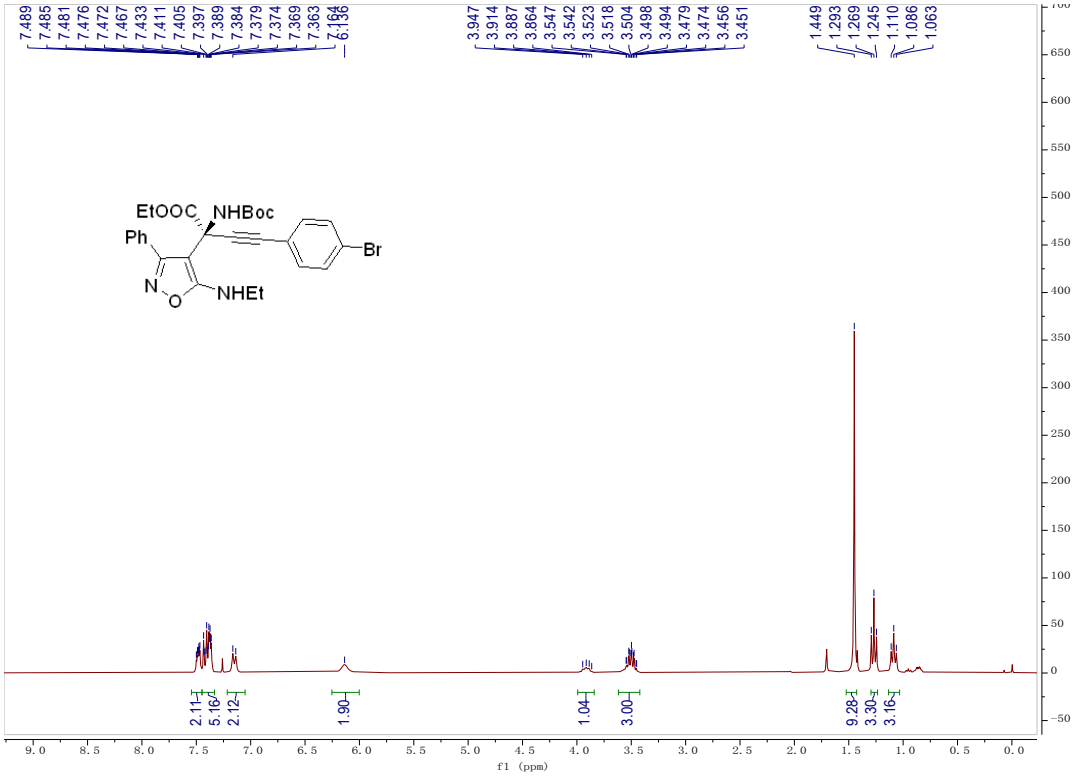


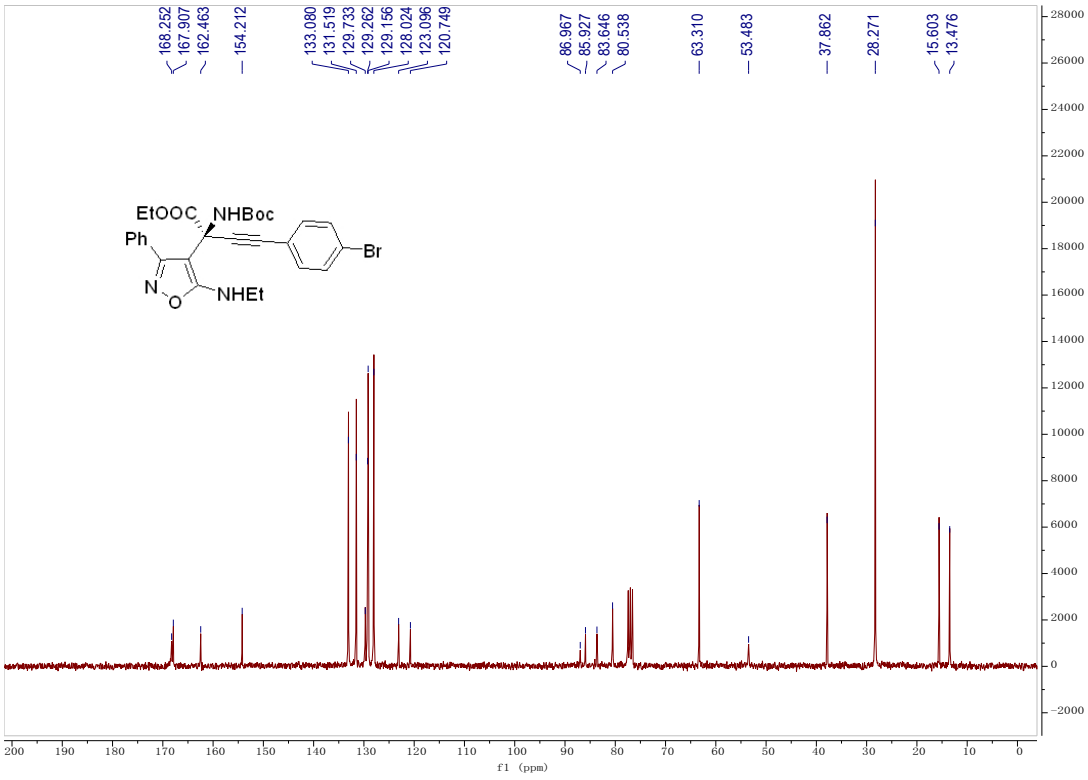
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ag)



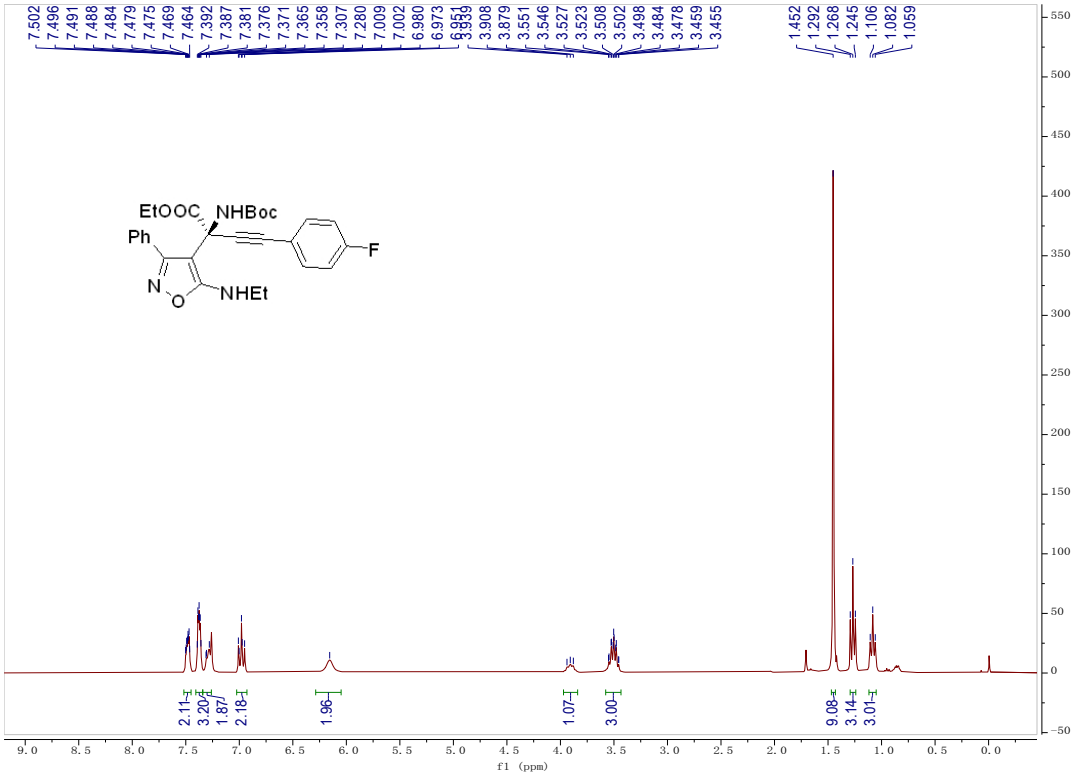


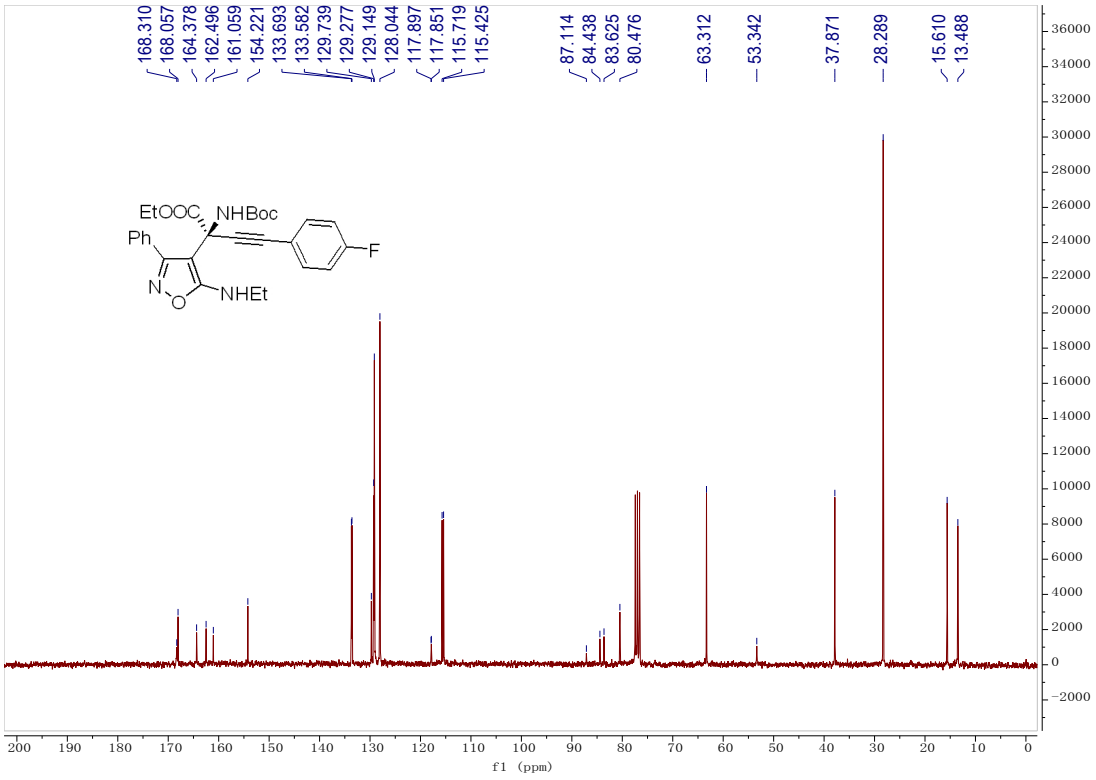
Ethyl (*S*)-4-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ah)



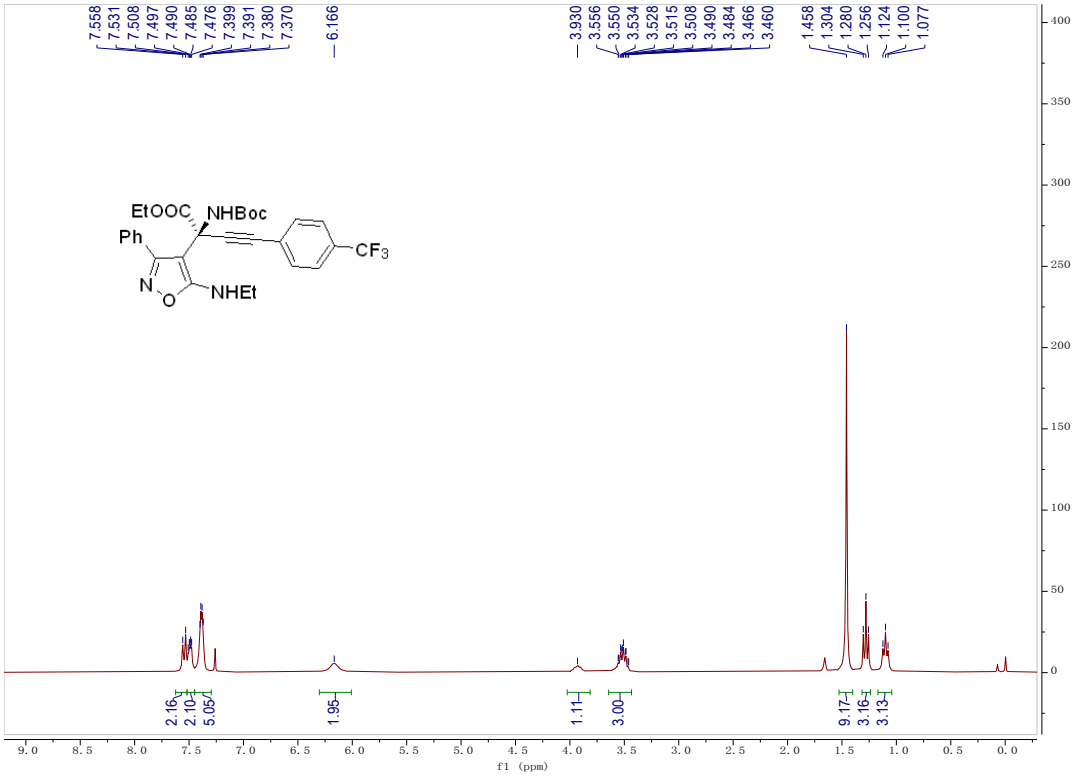


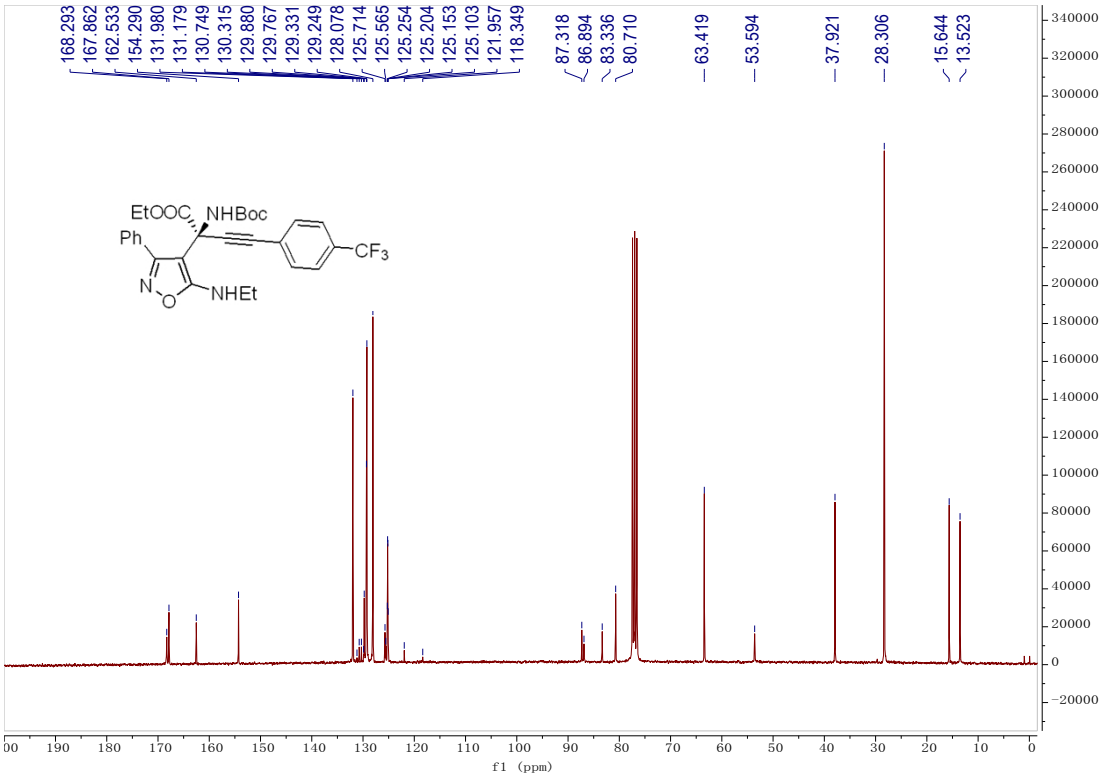
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-fluorophenyl)but-3-ynoate (3ai)



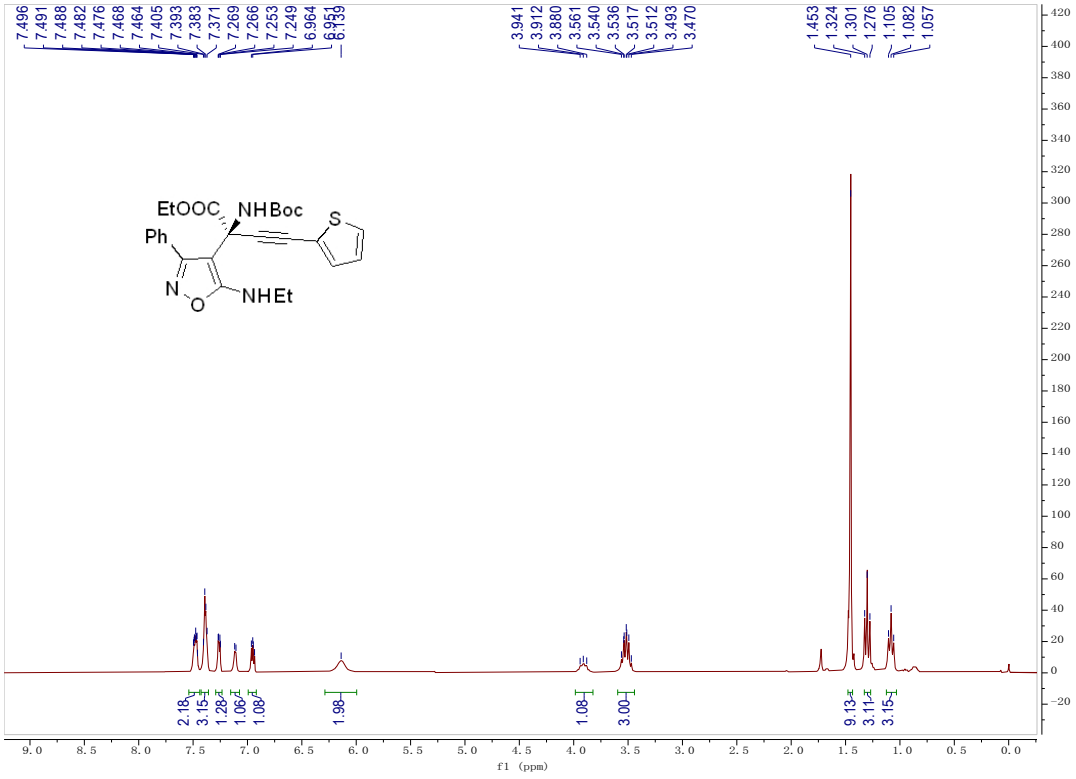


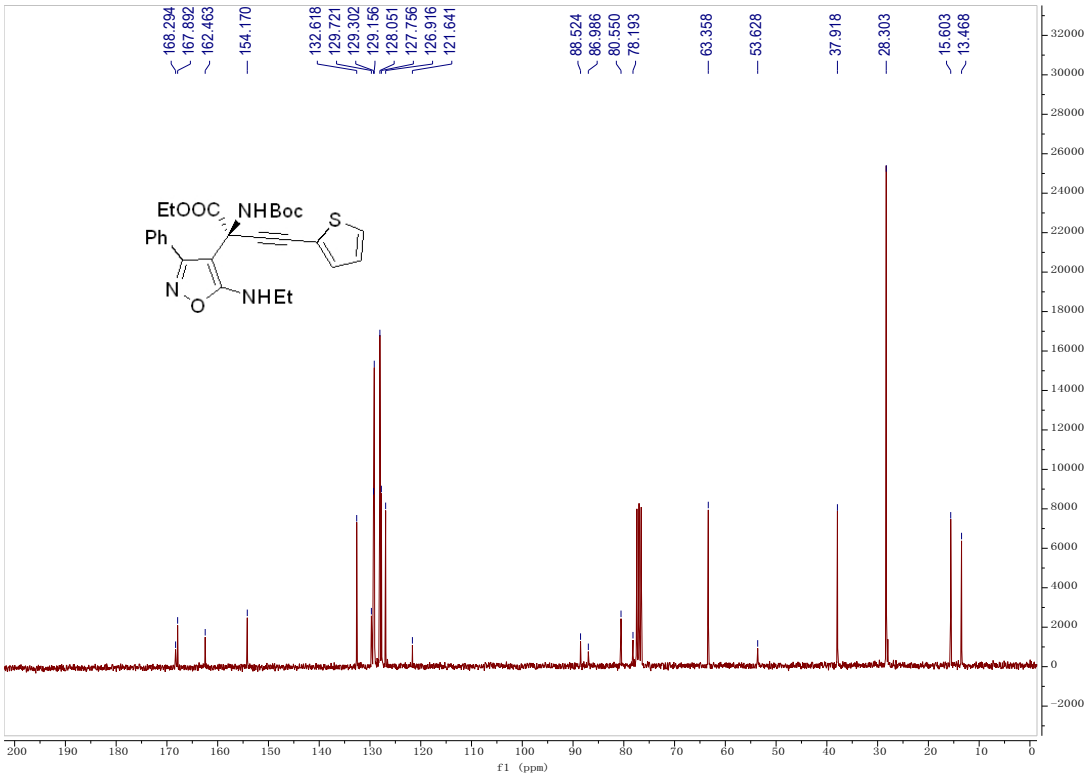
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-(trifluoromethyl)phenyl)but-3-ynoate (3aj)



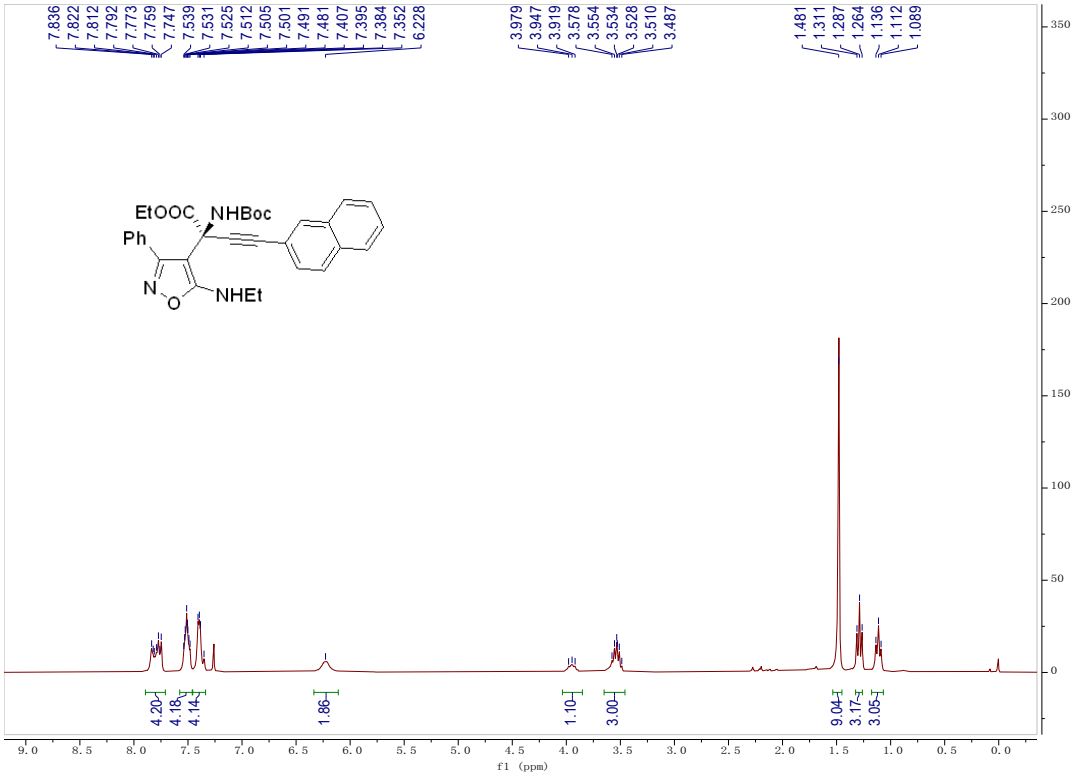


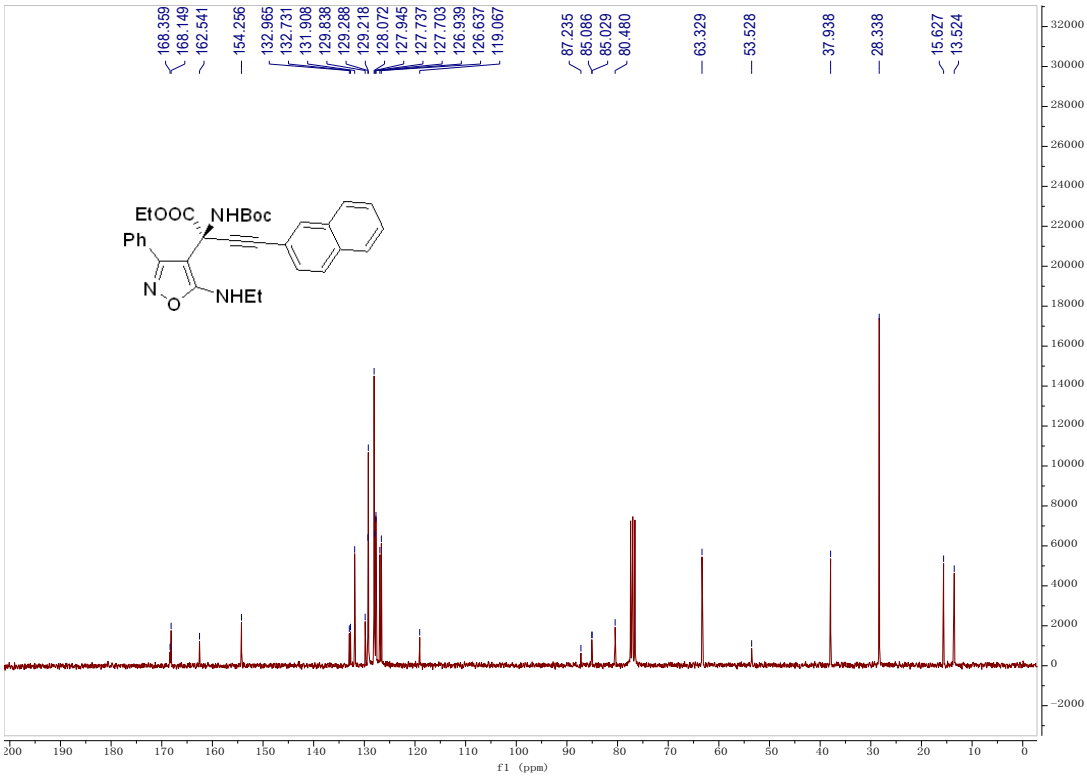
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(thiophen-2-yl)but-3-ynoate (3ak)



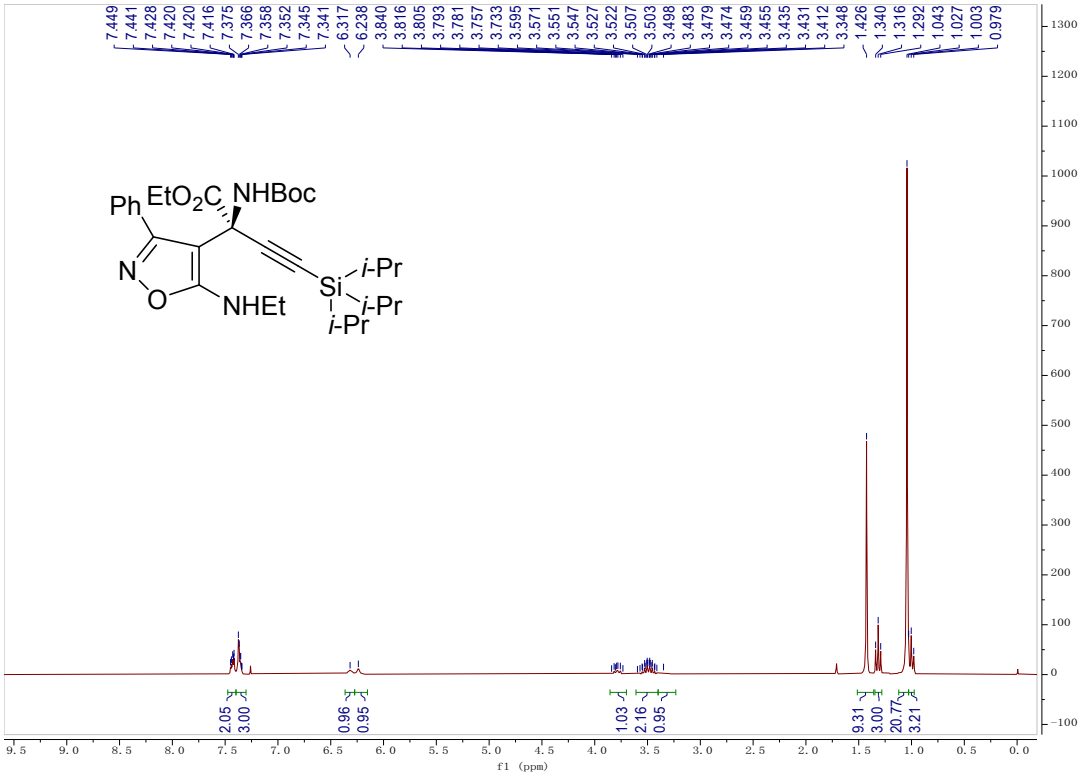


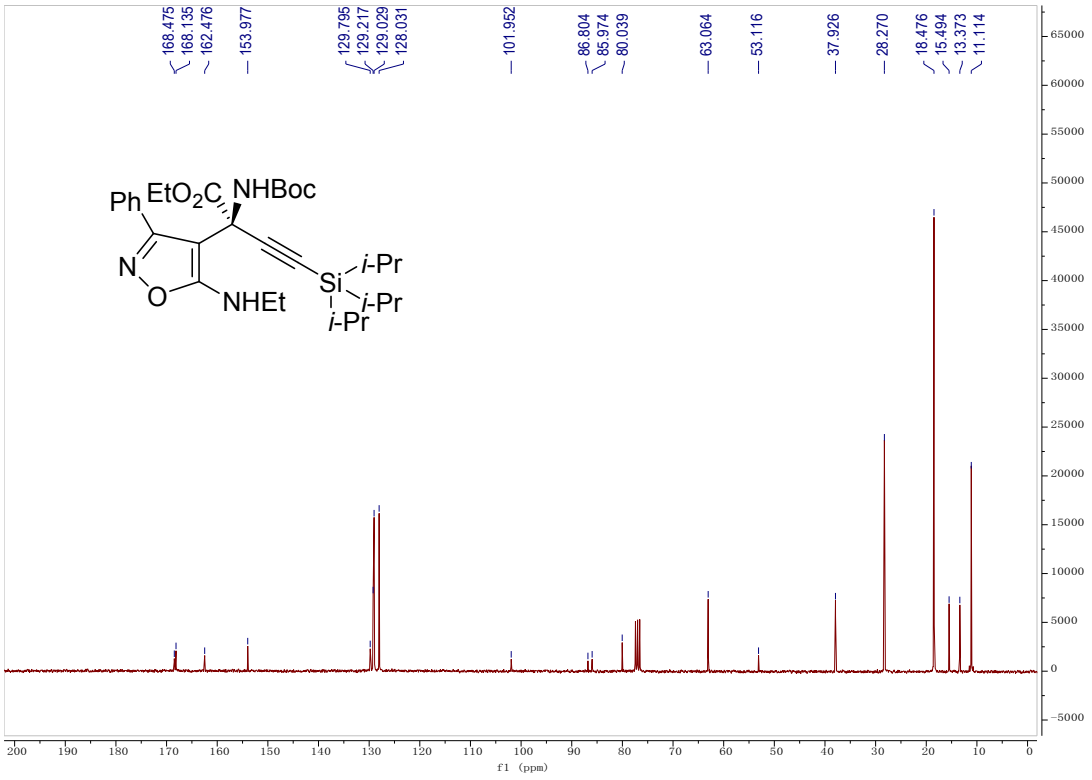
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(naphthalen-2-yl)but-3-ynoate (3al)



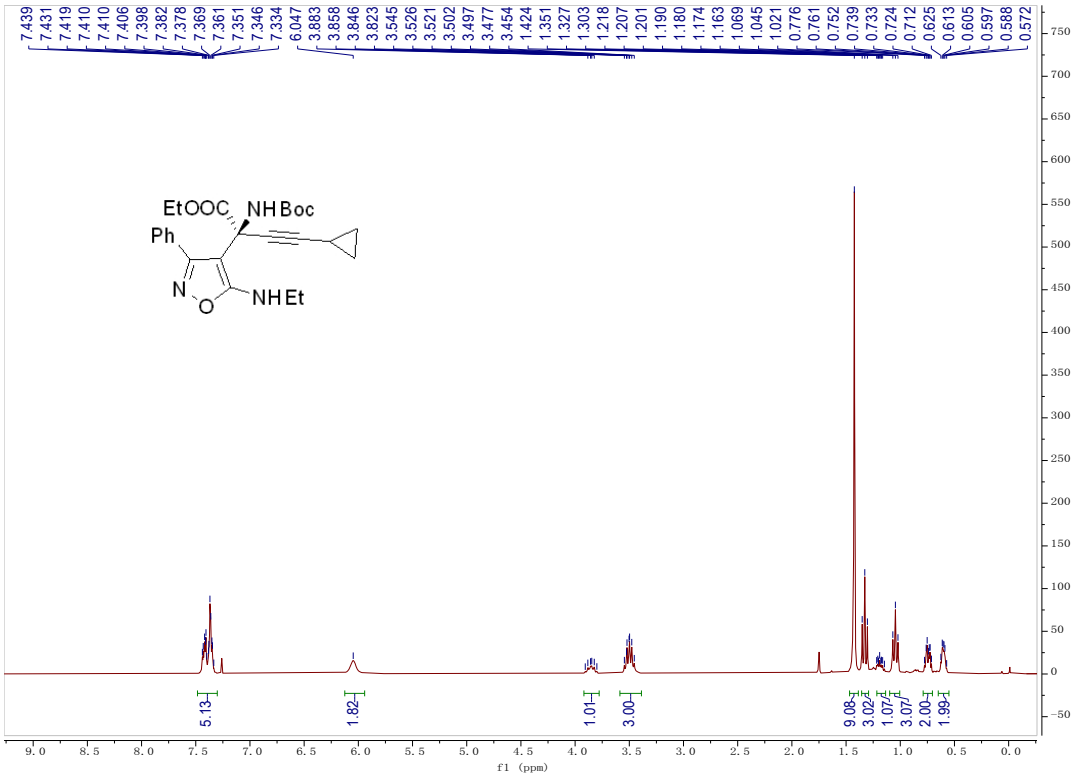


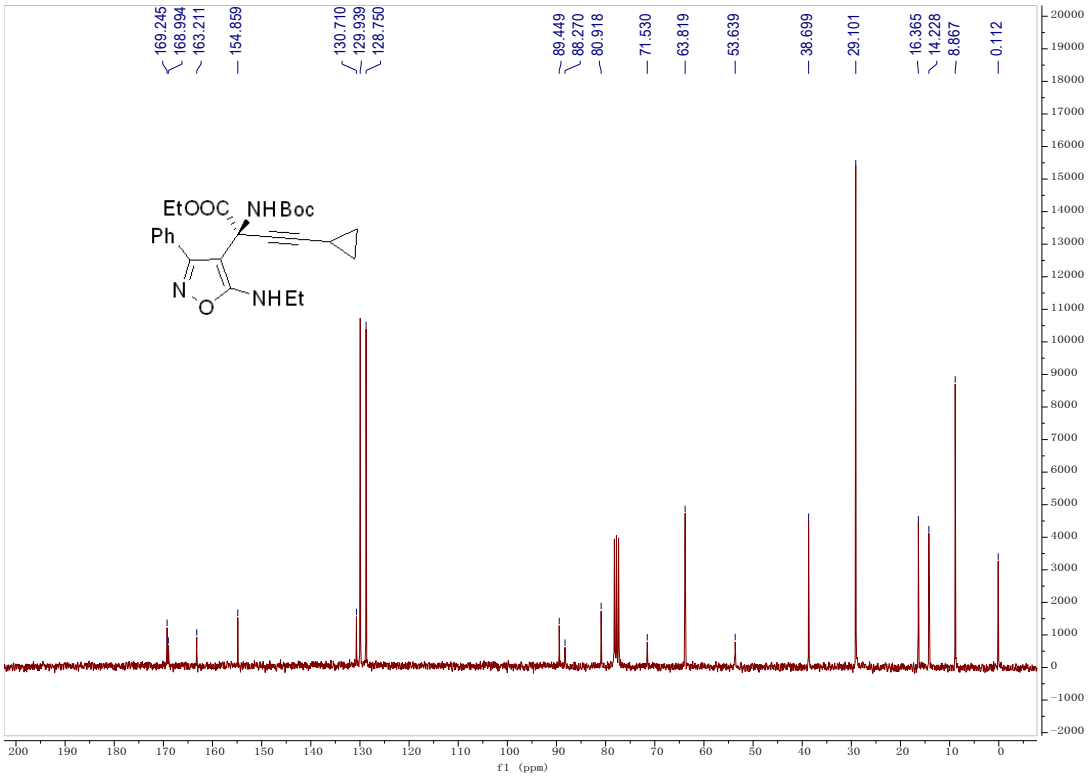
Ethyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(triisopropylsilyl)but-3-ynoate (3am)



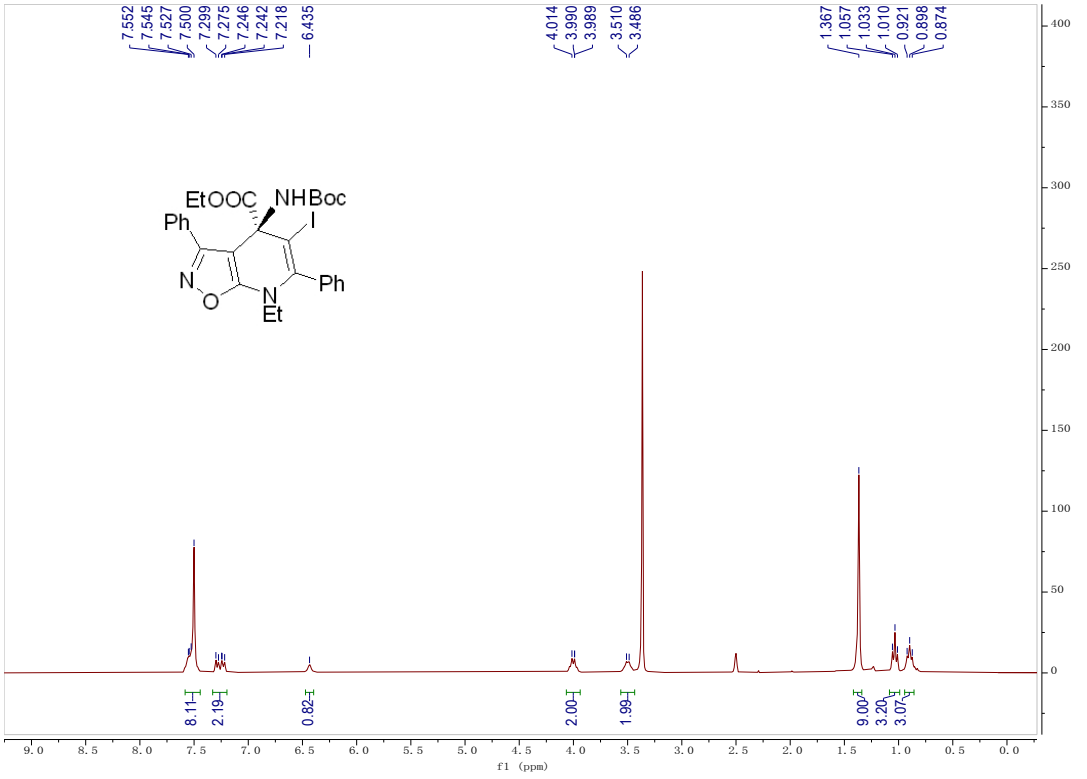


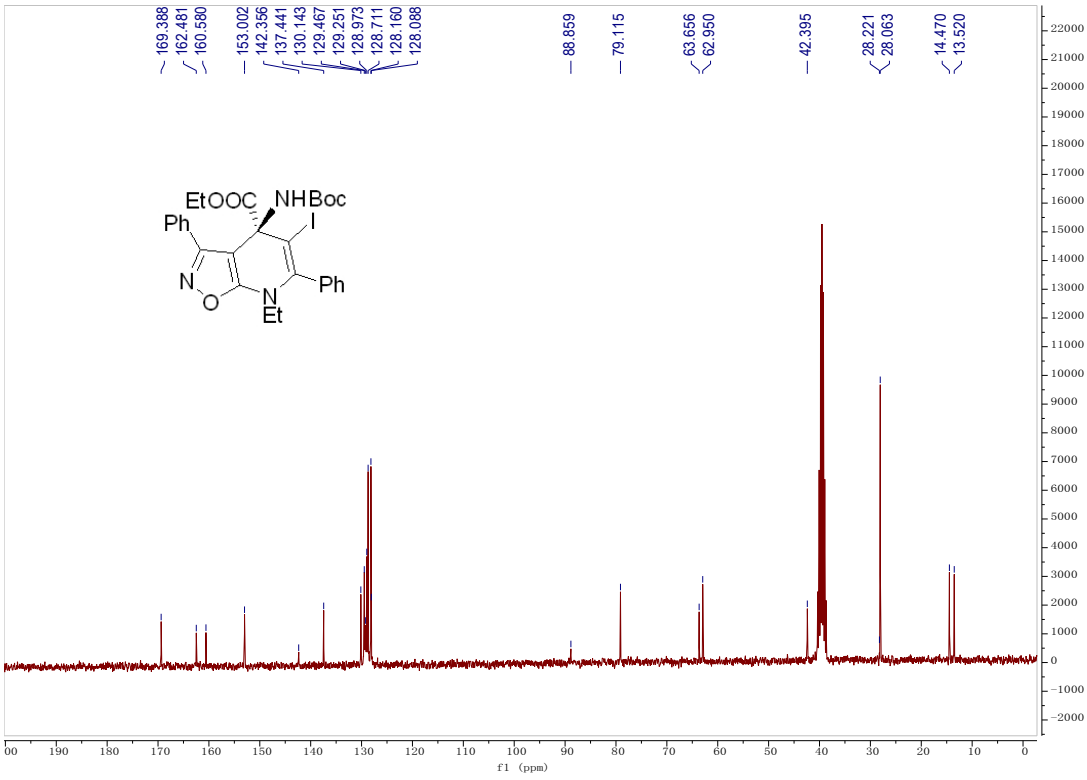
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-cyclopropyl-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3an)



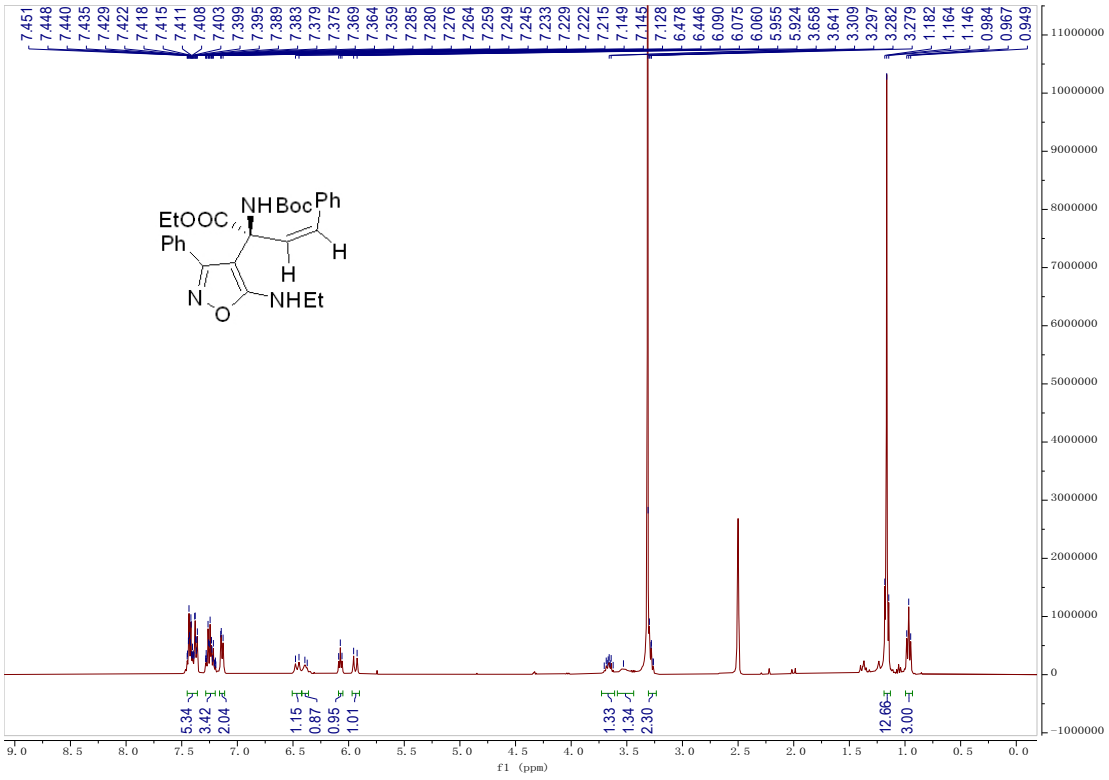


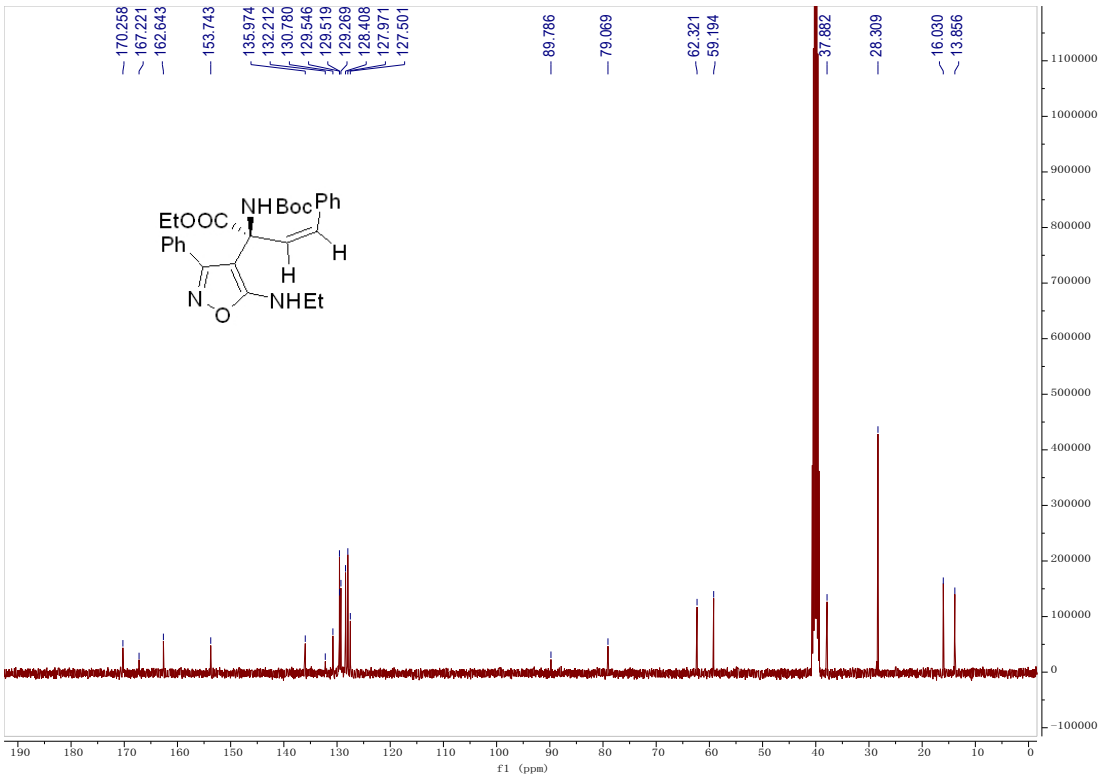
Ethyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-7-ethyl-5-iodo-3,6-diphenyl-4,7-dihydroisoxazolo[5,4-b]pyridine-4-carboxylate (4)



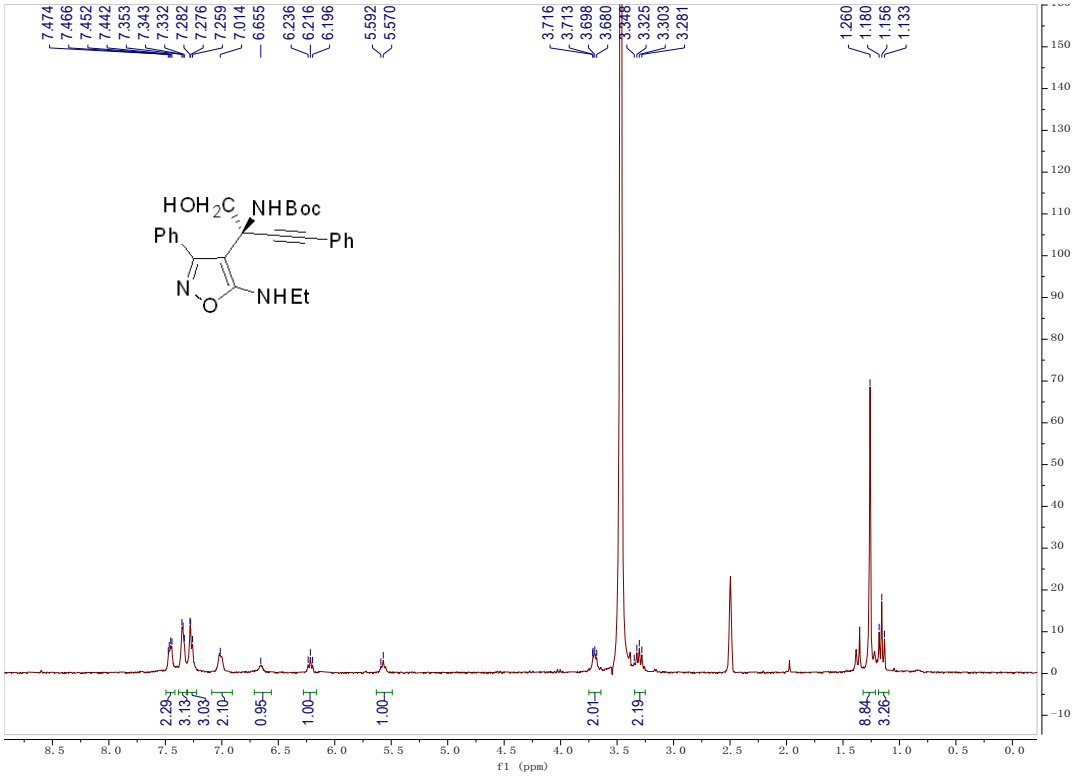


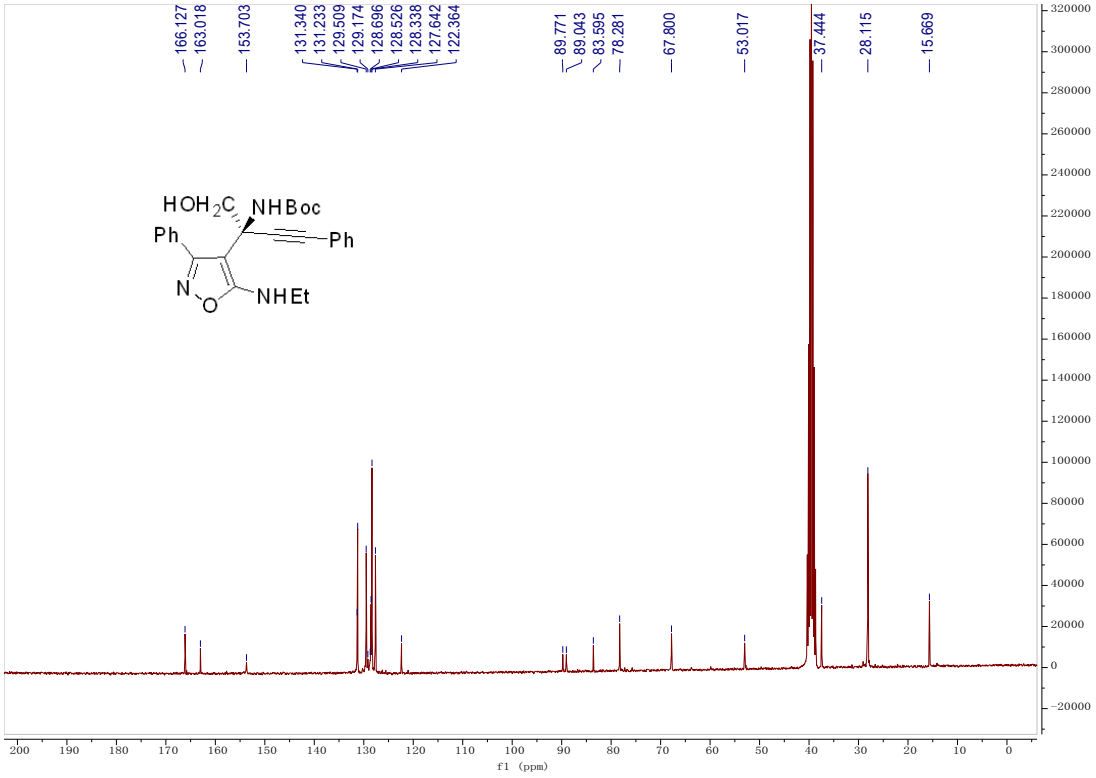
Ethyl (*S*,*Z*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-phenylbut-3-enoate (5)



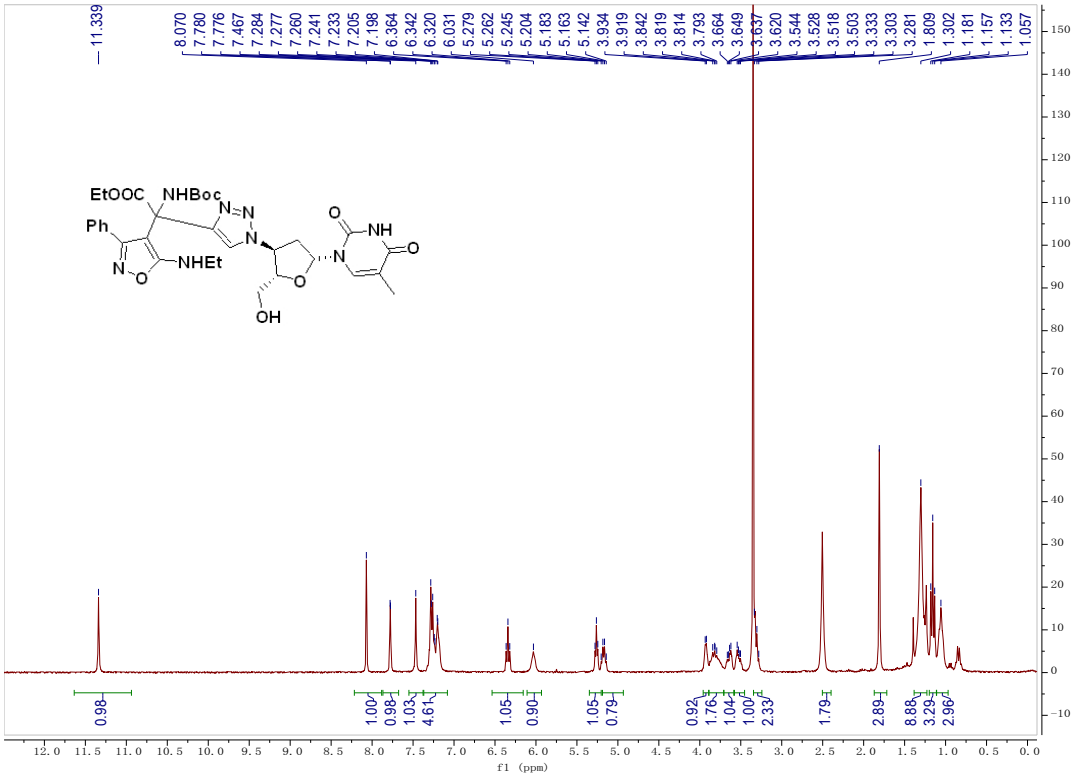


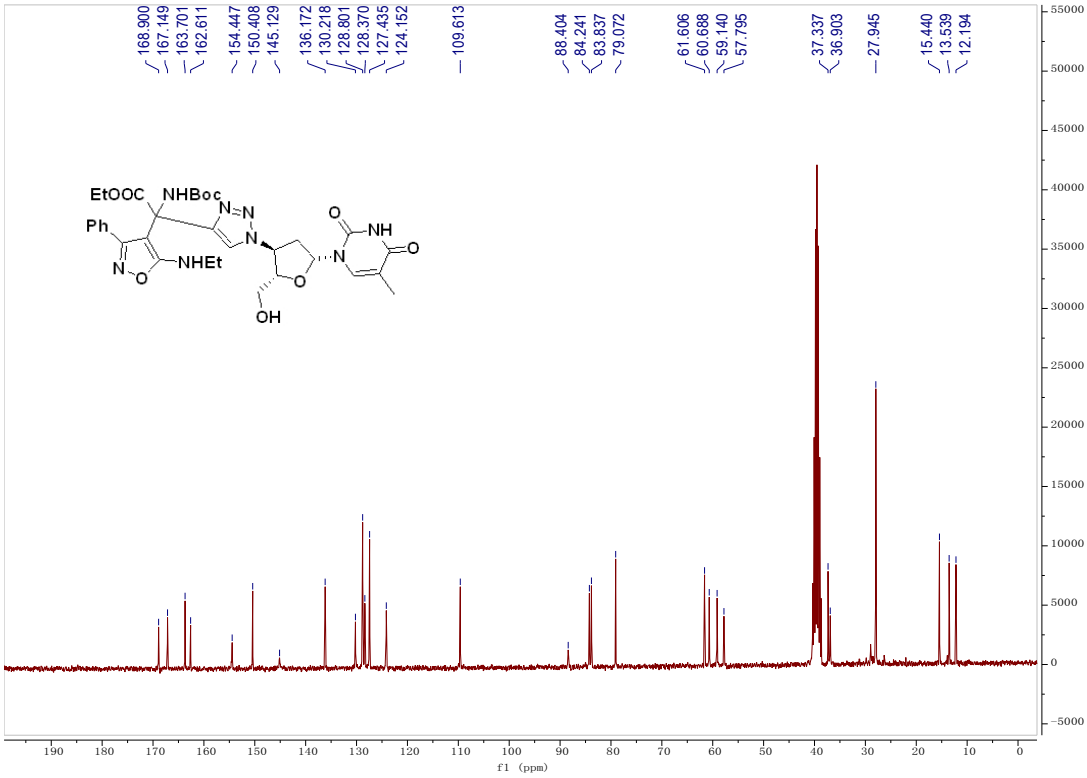
tert-butyl (_S_)-(2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-1-hydroxy-4-phenylbut-3-yn-2-yl)carbamate (6)





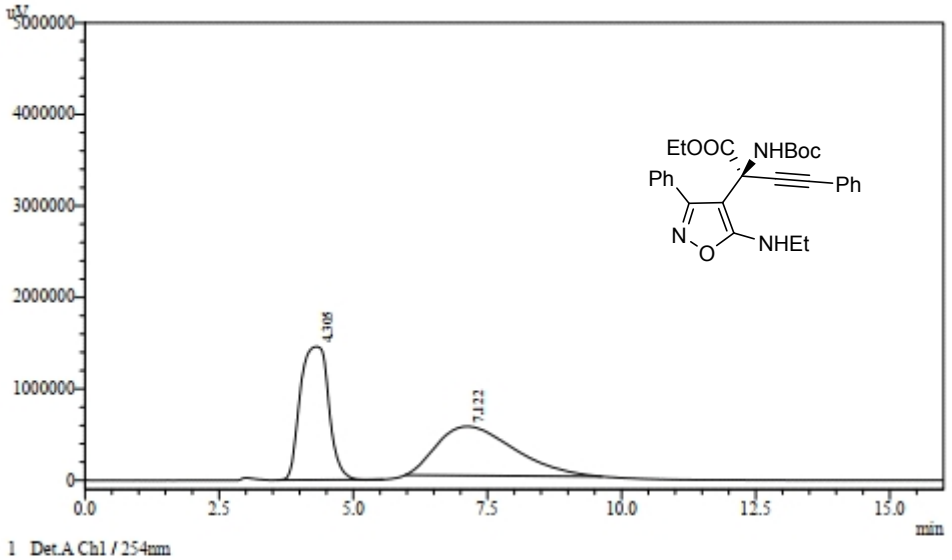
Ethyl 2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-2-(1-((2*S*,3*S*,5*R*)-2-(hydroxymethyl)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3-yl)-1H-1,2,3-triazol-4-yl)acetate (8)





6. HPLC Charts of Products

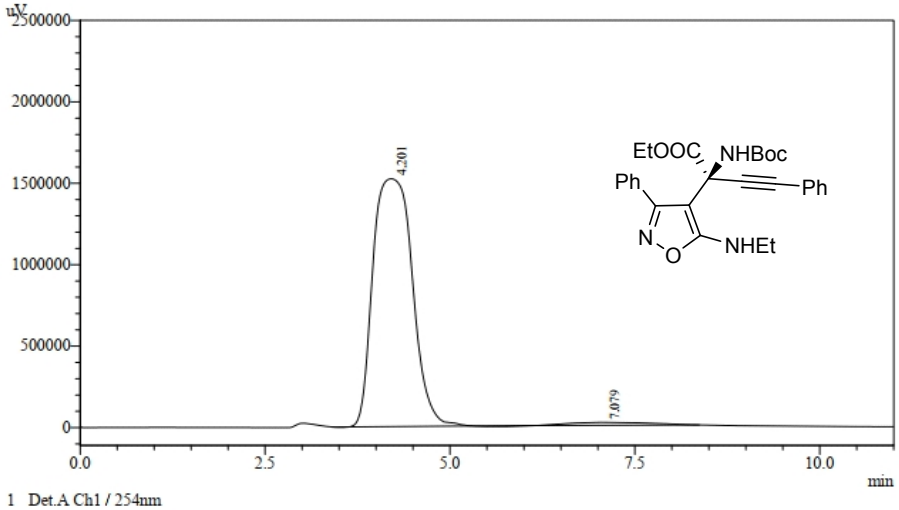
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-phenylbut-3-ynoate (3aa)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.305	53715356	1455787	49.838	73.070
2	7.122	54063761	536522	50.162	26.930
Total		107779117	1992308	100.000	100.000

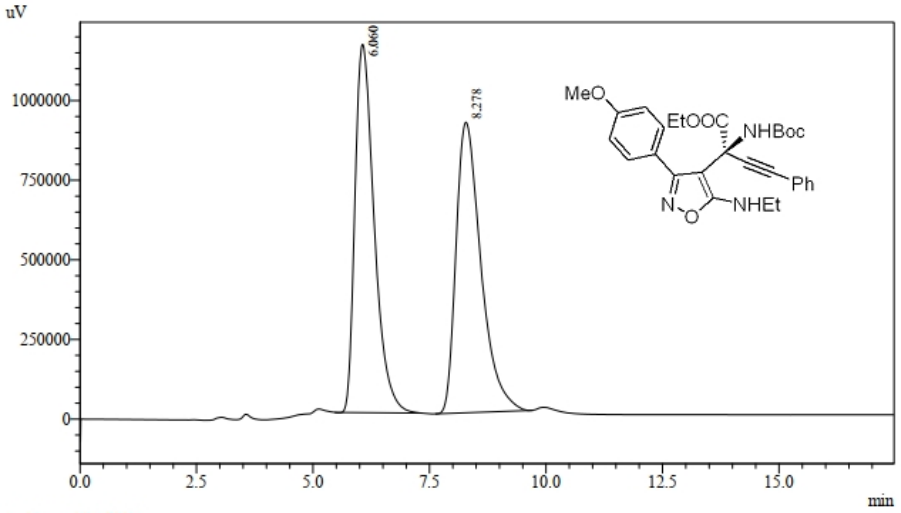


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.201	56253191	1521237	97.540	98.815
2	7.079	1418770	18250	2.460	1.185
Total		57671961	1539487	100.000	100.000

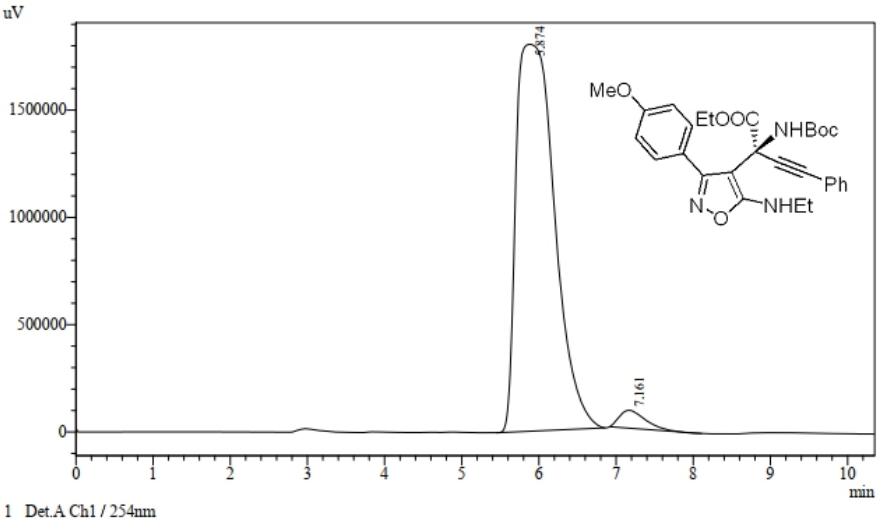
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ba)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.060	33252687	1155896	49.548	55.901
2	8.278	33859690	911866	50.452	44.099
Total		67112377	2067762	100.000	100.000

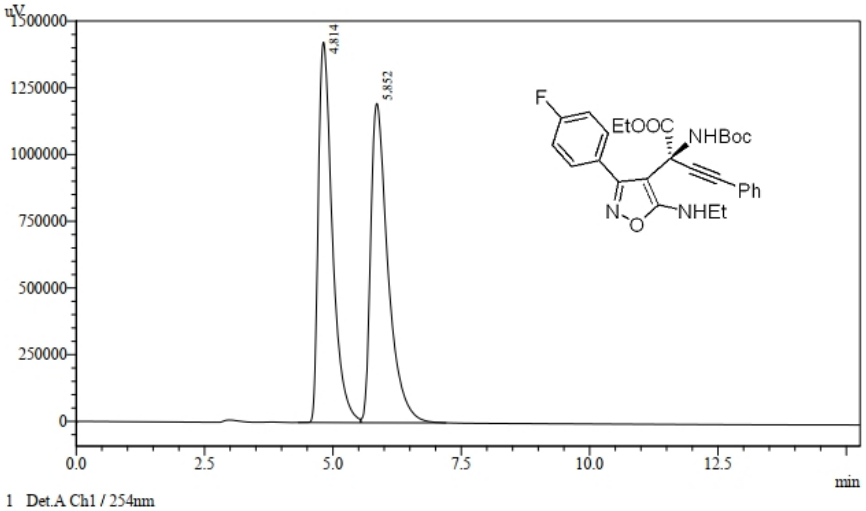


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.874	62626802	1803226	96.987	95.591
2	7.161	1945871	83169	3.013	4.409
Total		64572673	1886395	100.000	100.000

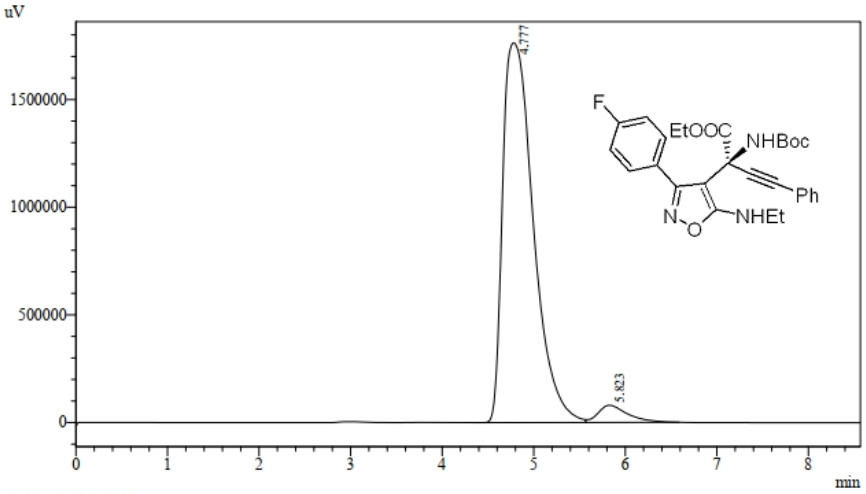
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-fluorophenyl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ca)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.814	27209407	1425297	49.227	54.365
2	5.852	28064324	1196402	50.773	45.635
Total		55273731	2621699	100.000	100.000

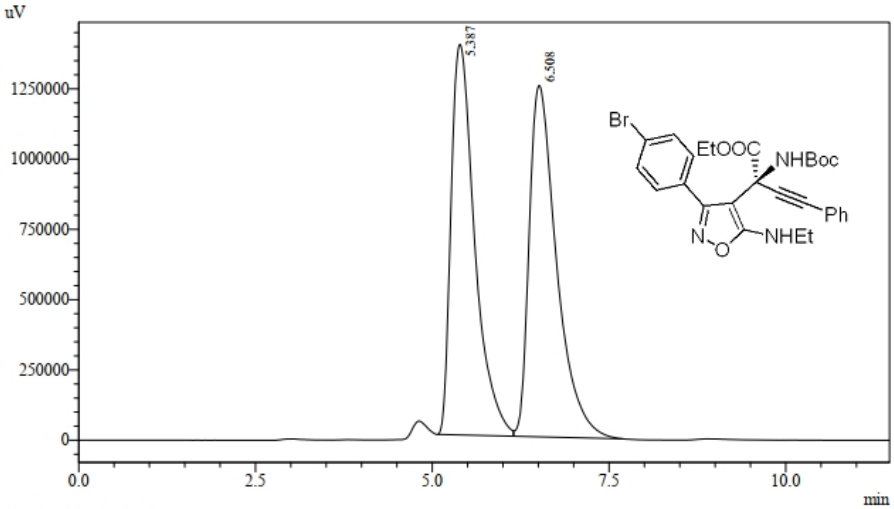


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.777	41128318	1762858	95.816	95.672
2	5.823	1796047	79746	4.184	4.328
Total		42924365	1842604	100.000	100.000

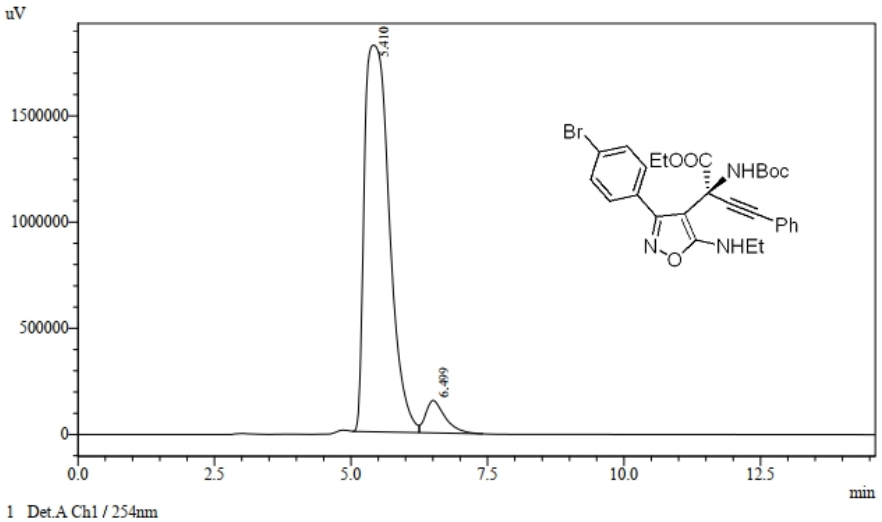
Ethyl (*S*)-2-(3-(4-bromophenyl)-5-(ethylamino)isoxazol-4-yl)-2-((*tert*-butoxycarbonyl)amino)-4-phenylbut-3-ynoate (3da)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.387	32437980	1389399	49.026	52.648
2	6.508	33726825	1249634	50.974	47.352
Total		66164805	2639033	100.000	100.000

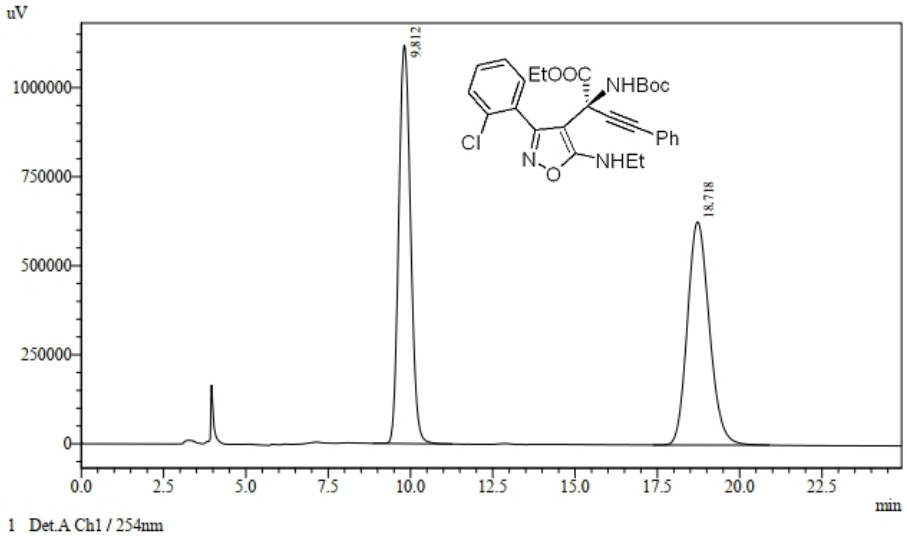


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.410	57932818	1819835	93.850	92.261
2	6.499	3796038	152659	6.150	7.739
Total		61728856	1972494	100.000	100.000

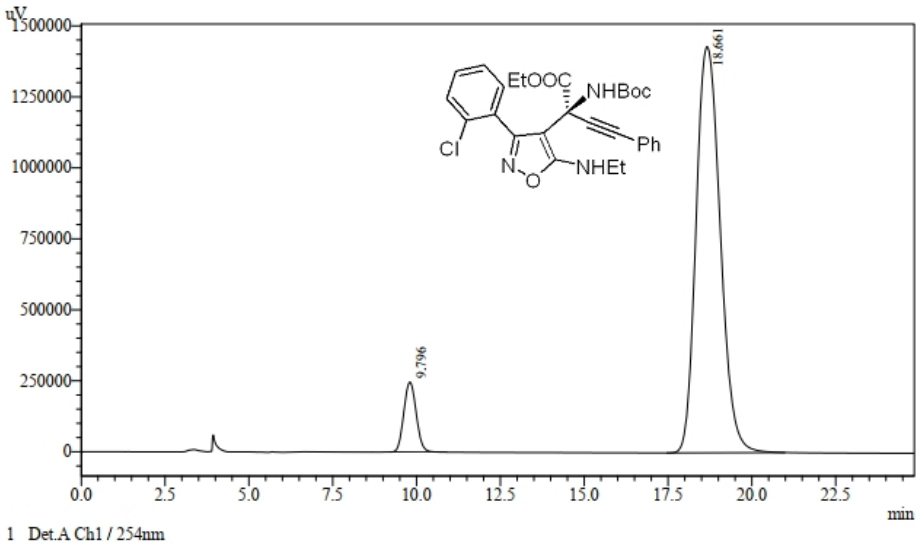
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(2-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ea)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.812	27981707	1117960	49.066	64.088
2	18.718	29046927	626462	50.934	35.912
Total		57028634	1744422	100.000	100.000

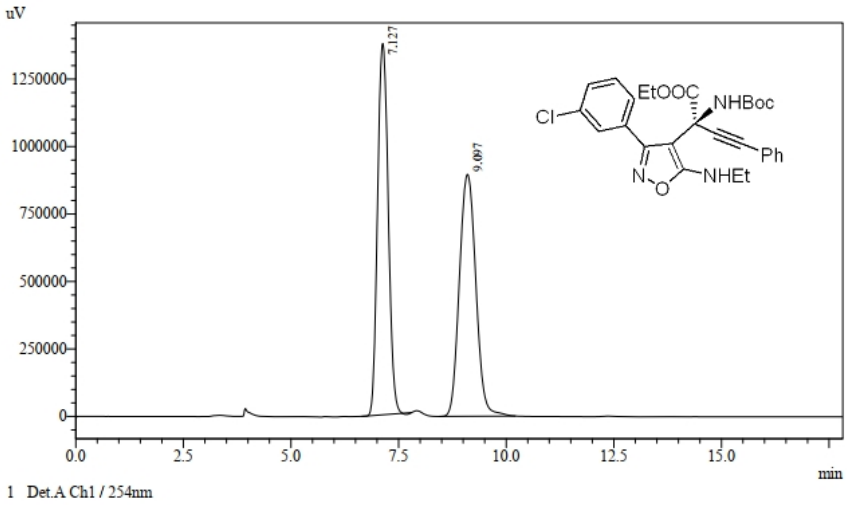


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.796	6351622	246362	8.145	14.693
2	18.661	71633435	1430372	91.855	85.307
Total		77985057	1676735	100.000	100.000

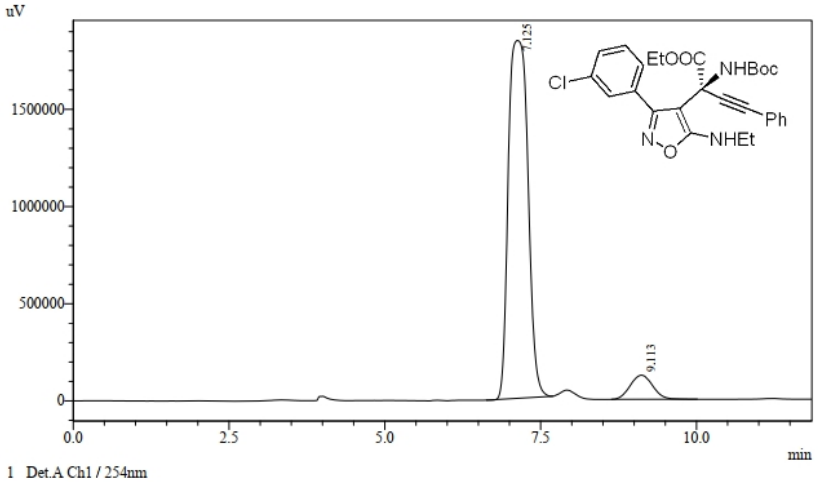
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(3-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3fa)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.127	23684078	1375268	49.789	60.531
2	9.097	23885258	896733	50.211	39.469
Total		47569336	2272001	100.000	100.000

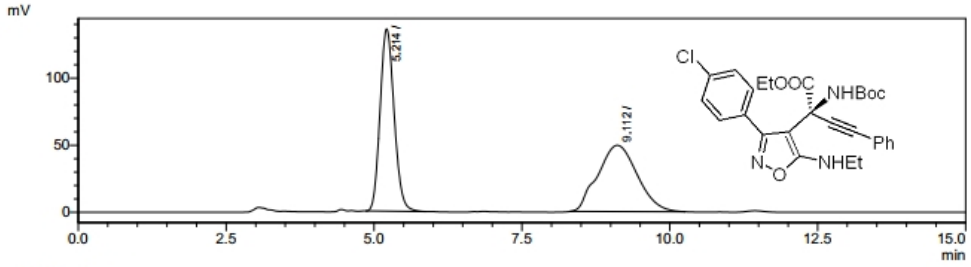


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

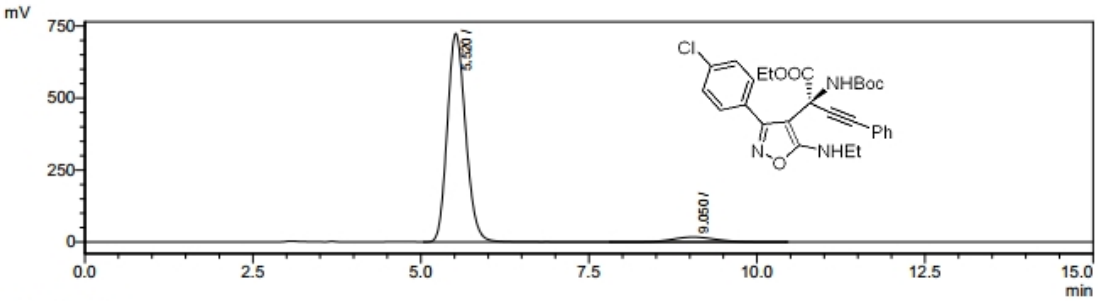
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.125	40266528	1841327	92.797	93.676
2	9.113	3125655	124302	7.203	6.324
Total		43392183	1965629	100.000	100.000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(3-(4-chlorophenyl)-5-(ethylamino) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ga)



检测器A 254nm

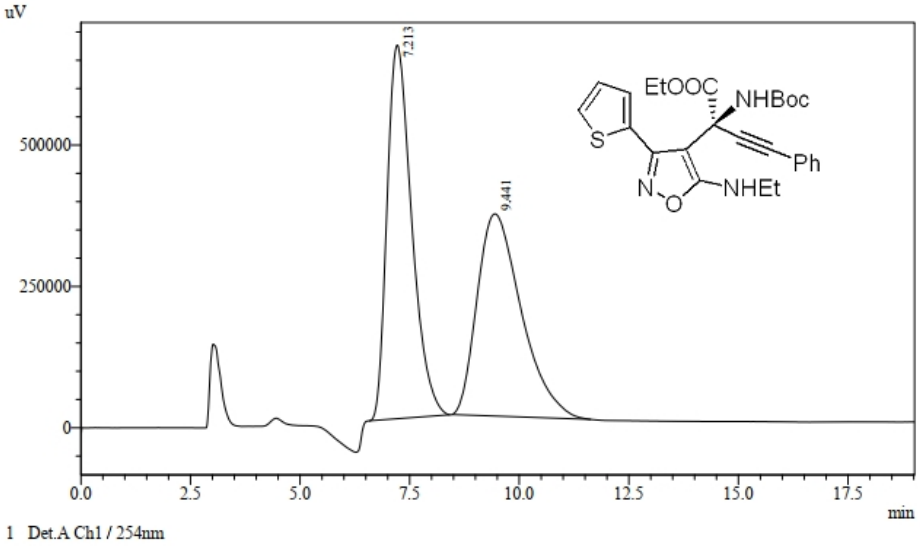
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.214	2244847	49.437	135829	73.353	49.437		M		
2	9.112	2295946	50.563	49342	26.647	50.563		M		
总计		4540792	100.000	185171	100.000					



检测器A 254nm

Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.520	13826611	94.793	724231	97.693	94.793		S		
2	9.050	759530	5.207	17099	2.307	5.207		T		
总计		14586141	100.000	741330	100.000					

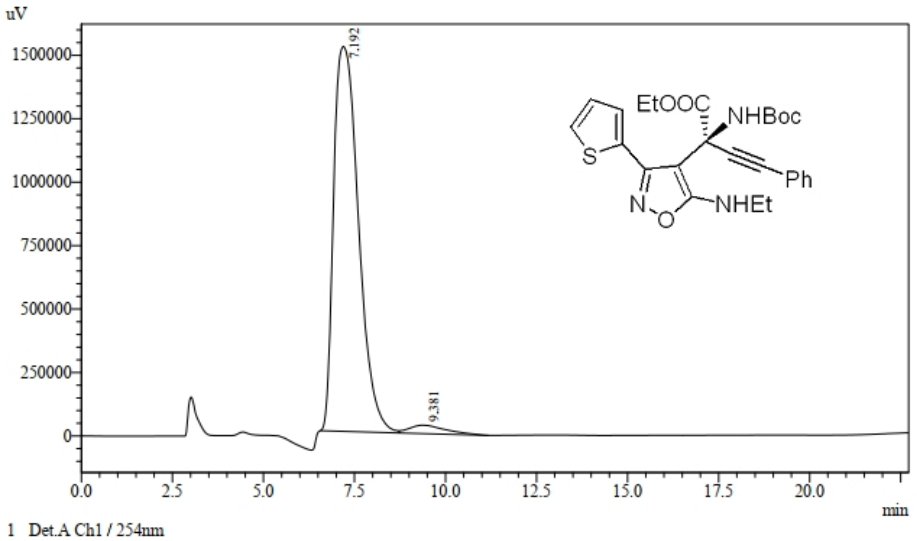
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(thiophen-2-yl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ha)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.213	25874649	660758	50.752	64.890
2	9.441	25107866	357511	49.248	35.110
Total		50982515	1018268	100.000	100.000

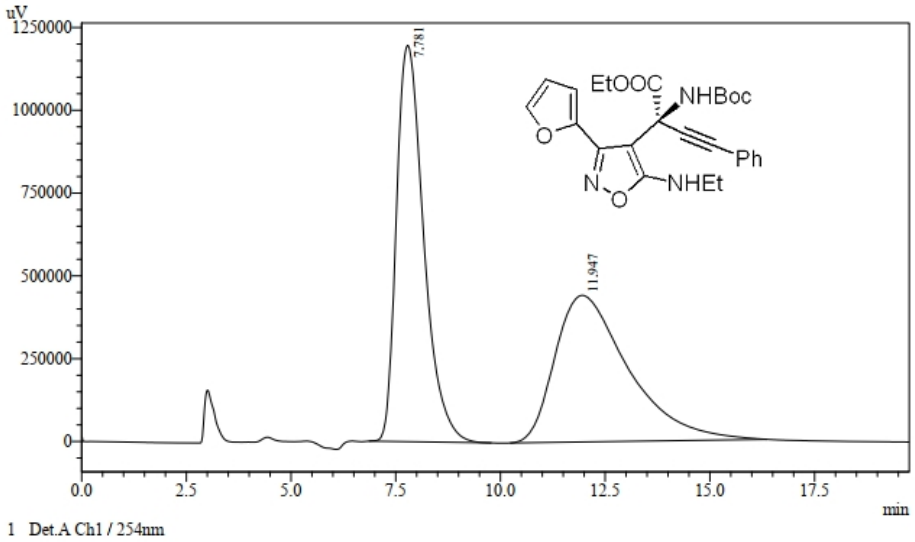


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.192	71961416	1516233	96.862	97.856
2	9.381	2331039	33218	3.138	2.144
Total		74292455	1549451	100.000	100.000

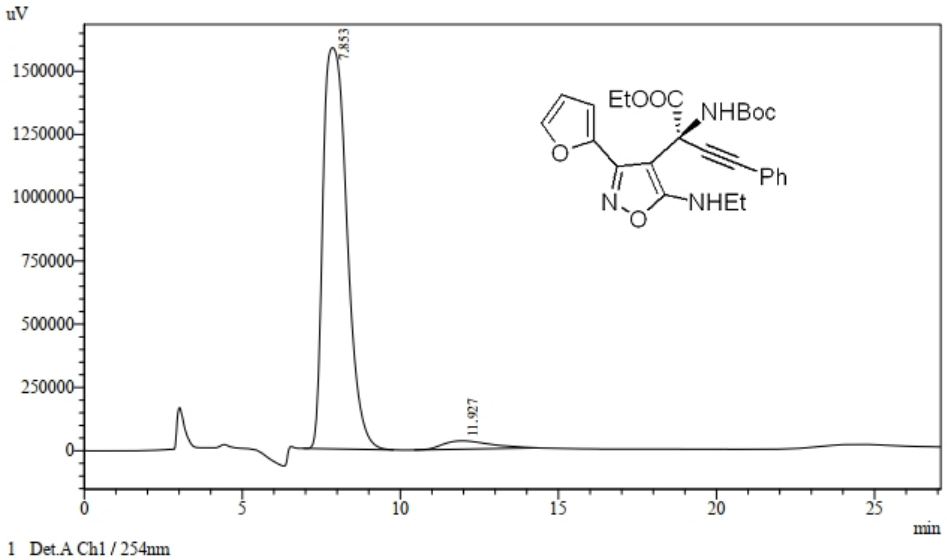
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(furan-2-yl) isoxazol-4-yl)-4-phenylbut-3-ynoate (3ia)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.781	54288322	1196355	50.154	73.000
2	11.947	53954565	442483	49.846	27.000
Total		108242887	1638837	100.000	100.000

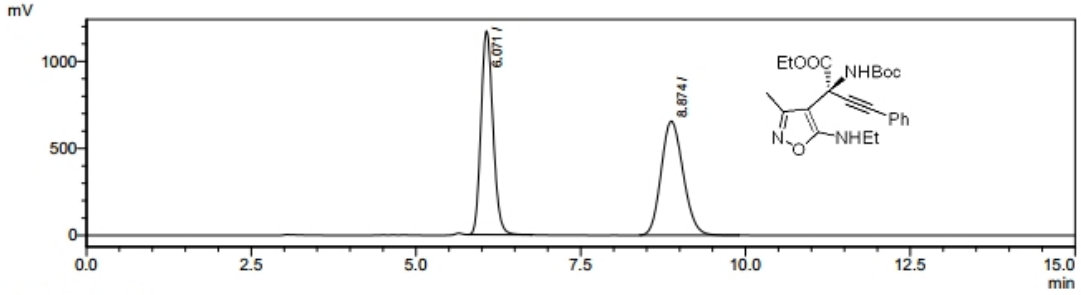


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

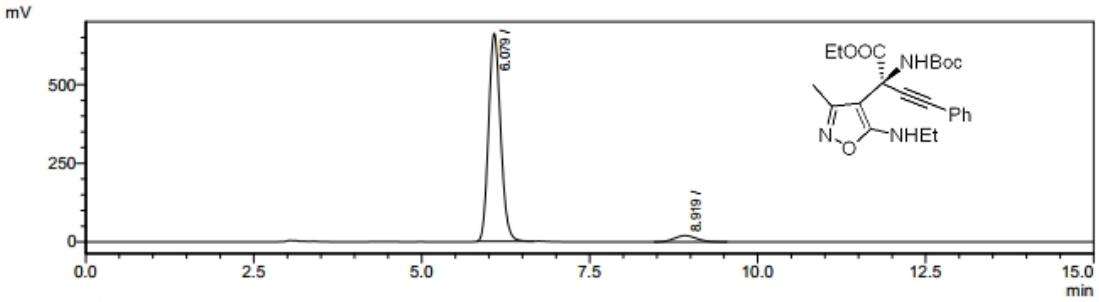
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.853	83632165	1585438	96.051	97.975
2	11.927	3438634	32772	3.949	2.025
Total		87070798	1618210	100.000	100.000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-methylisoxazol-4-yl)-4-phenylbut-3-ynoate (3ja)



检测器A 254nm

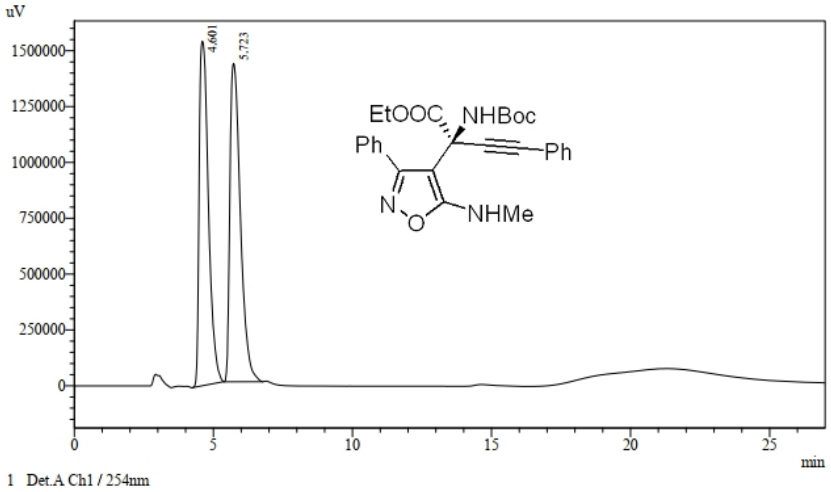
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	6.071	14859561	49.341	1170813	64.125	49.341		M		
2	8.874	15256283	50.659	655025	35.875	50.659		M		
总计		30115844	100.000	1825838	100.000					



检测器A 254nm

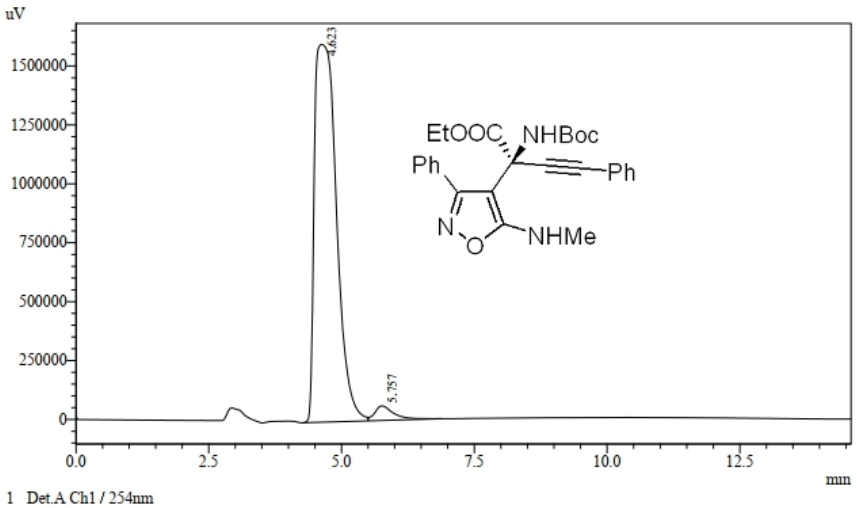
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	6.079	8234993	94.782	661034	97.077	94.782		M		
2	8.919	453370	5.218	19907	2.923	5.218		M		
总计		8688363	100.000	680941	100.000					

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(methylamino)-3-phenylisoxazol -4-yl)-4-phenylbut-3-ynoate (3la)



Detector A Ch1 254nm

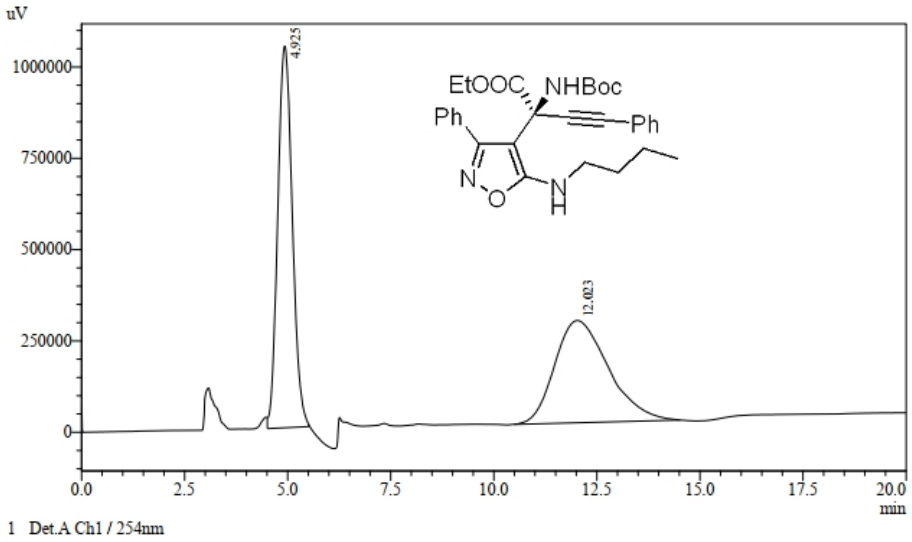
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.601	35707236	1541760	48.844	51.975
2	5.723	37396748	1424574	51.156	48.025
Total		73103984	2966334	100.000	100.000



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.623	46250888	1602631	96.727	96.257
2	5.757	1565130	62314	3.273	3.743
Total		47816018	1664945	100.000	100.000

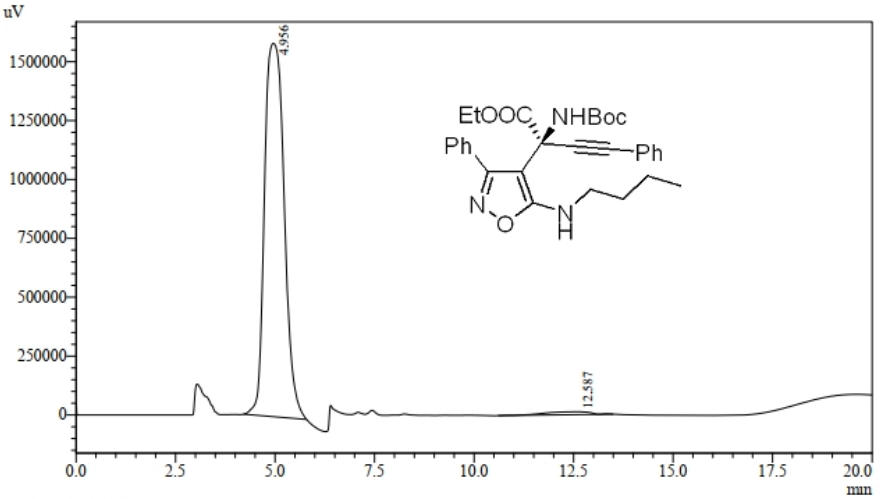
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(butylamino)-3-phenylisoxazol -4-yl)-4-phenylbut-3-ynoate (3ma)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.925	25708825	1044633	50.344	78.872
2	12.023	25357121	279832	49.656	21.128
Total		51065946	1324465	100.000	100.000

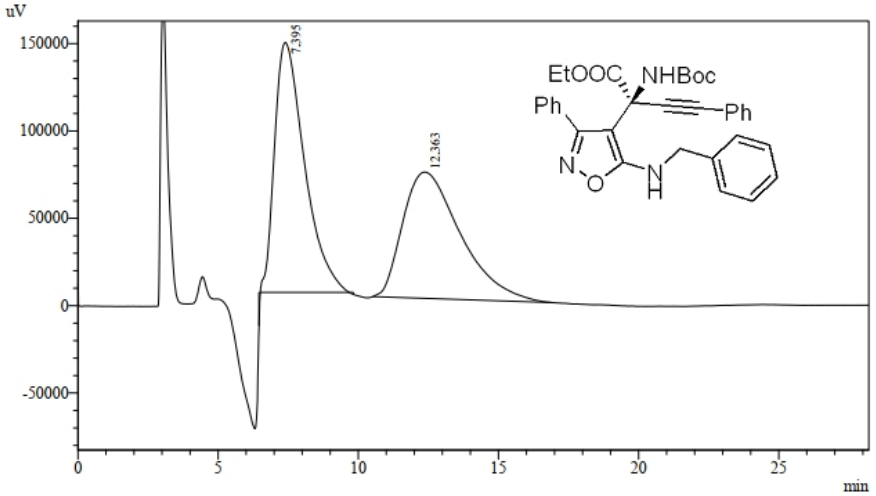


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.956	54481905	1584721	98.213	99.246
2	12.587	991151	12044	1.787	0.754
Total		55473055	1596765	100.000	100.000

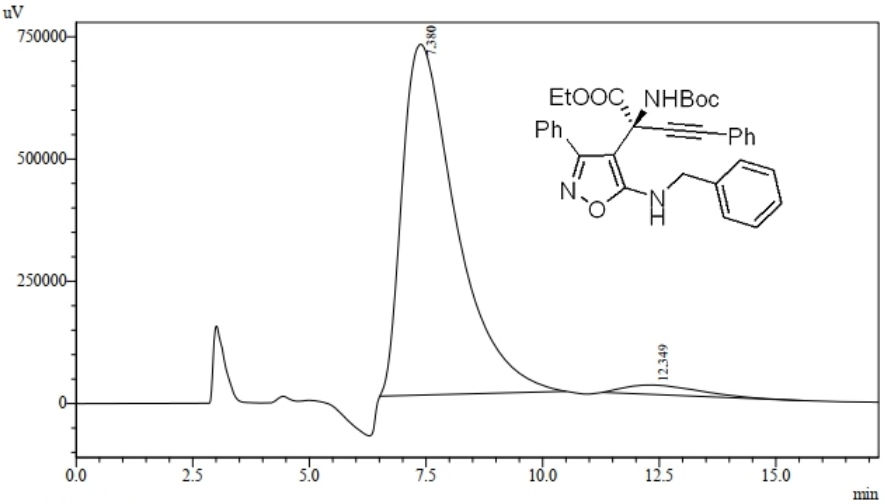
Ethyl (*S*)-2-(5-(benzylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl) amino)-4-phenylbut-3-ynoate (3na)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.395	10626764	143048	50.581	66.432
2	12.363	10382788	72283	49.419	33.568
Total		21009552	215330	100.000	100.000

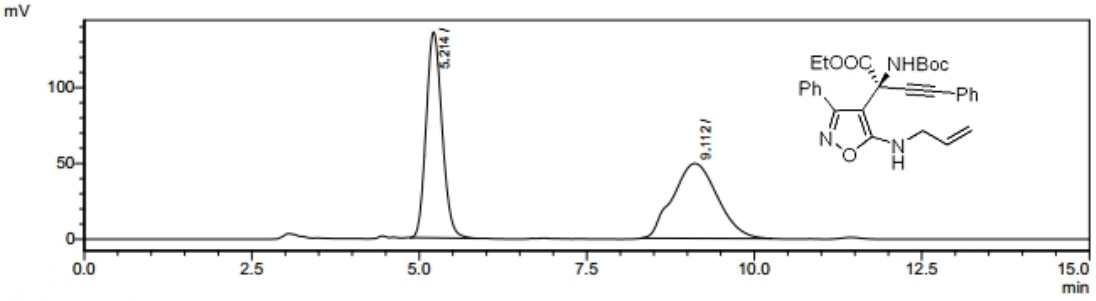


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

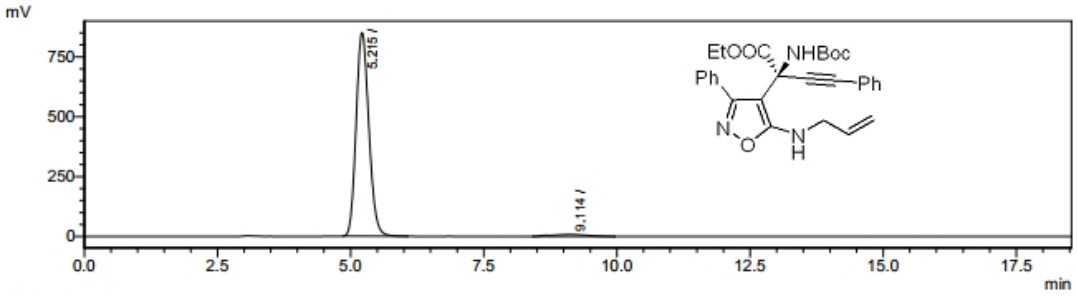
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.380	57815609	717490	96.387	97.374
2	12.349	2167395	19350	3.613	2.626
Total		59983005	736840	100.000	100.000

Ethyl (*S*)-2-(5-(allylamino)-3-phenylisoxazol-4-yl)-2-((*tert*-butoxycarbonyl) amino)-4-phenylbut-3-ynoate (3oa)



检测器A 254nm

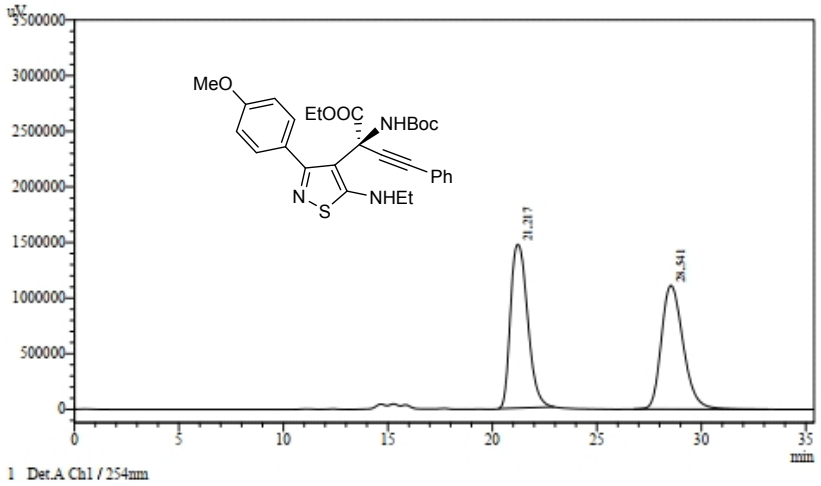
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.214	2244847	49.437	135829	73.353	49.437		M		
2	9.112	2295946	50.563	49342	26.647	50.563		M		
总计		4540792	100.000	185171	100.000					



检测器A 254nm

Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.215	14147904	97.441	850098	99.078	97.441		M		
2	9.114	371619	2.559	7907	0.922	2.559		M		
总计		14519522	100.000	858005	100.000					

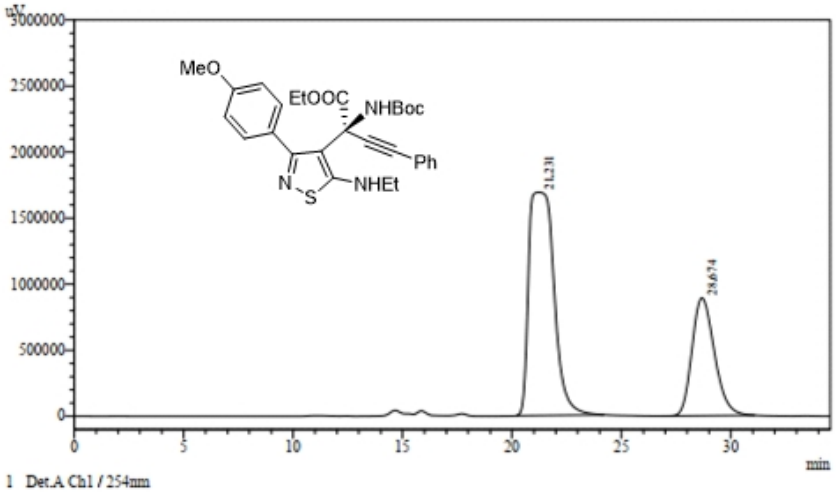
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-(4-methoxyphenyl)isothiazol-4-yl)-4-phenylbut-3-ynoate (3qa)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.217	84292336	1471914	50.967	56.956
2	28.541	81092490	1112388	49.033	43.044
Total		165384825	2584301	100.000	100.000

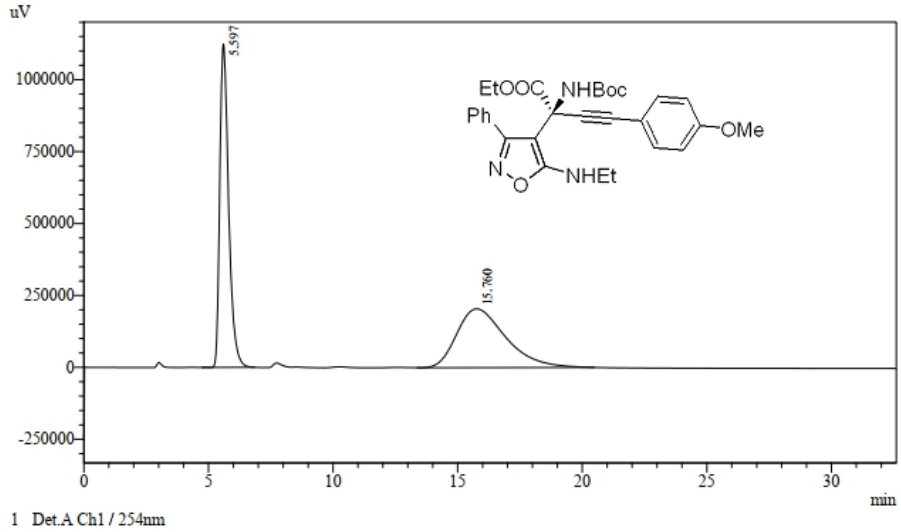


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.231	135900061	1689343	68.088	65.441
2	28.674	63694259	892126	31.912	34.559
Total		199594320	2581469	100.000	100.000

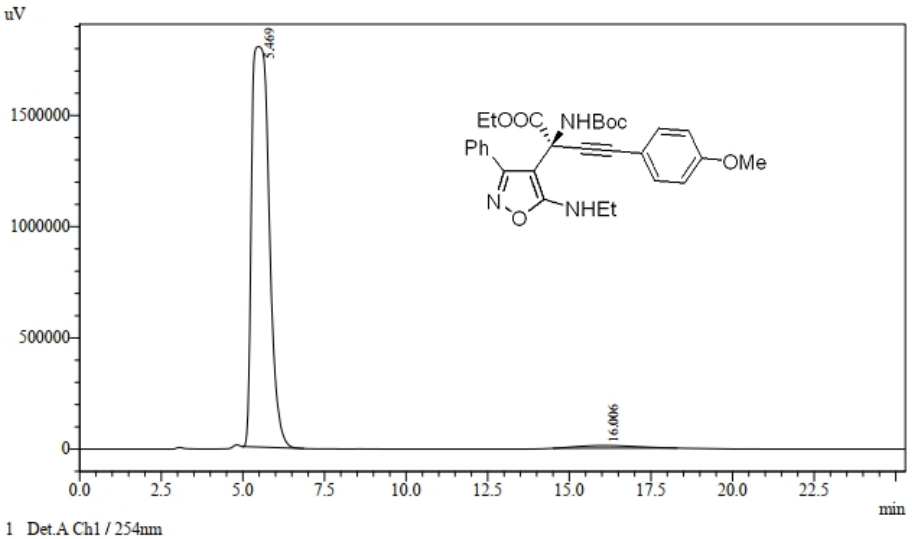
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-4-(4-methoxyphenyl)but-3-ynoate (3ab)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.597	27813238	1123497	49.837	84.625
2	15.760	27994932	204116	50.163	15.375
Total		55808170	1327613	100.000	100.000

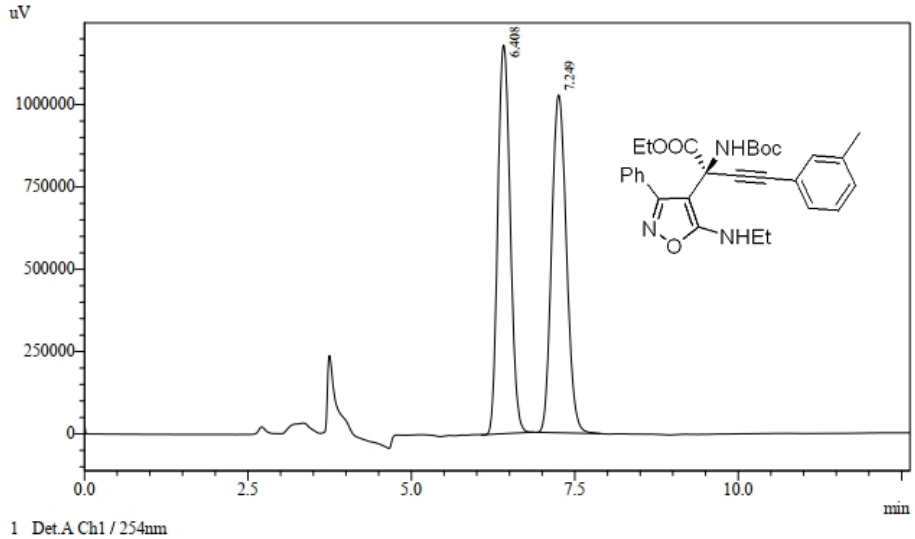


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.469	67354854	1799573	97.779	99.330
2	16.006	1530132	12141	2.221	0.670
Total		68884986	1811715	100.000	100.000

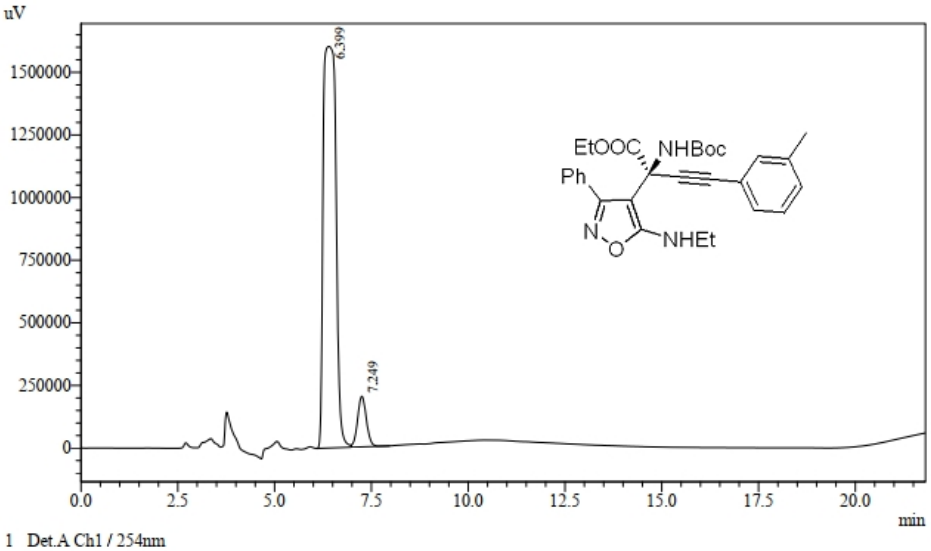
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(m-tolyl)but-3-ynoate (3ac)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.408	15595369	1179601	49.167	53.479
2	7.249	16123996	1026132	50.833	46.521
Total		31719365	2205734	100.000	100.000

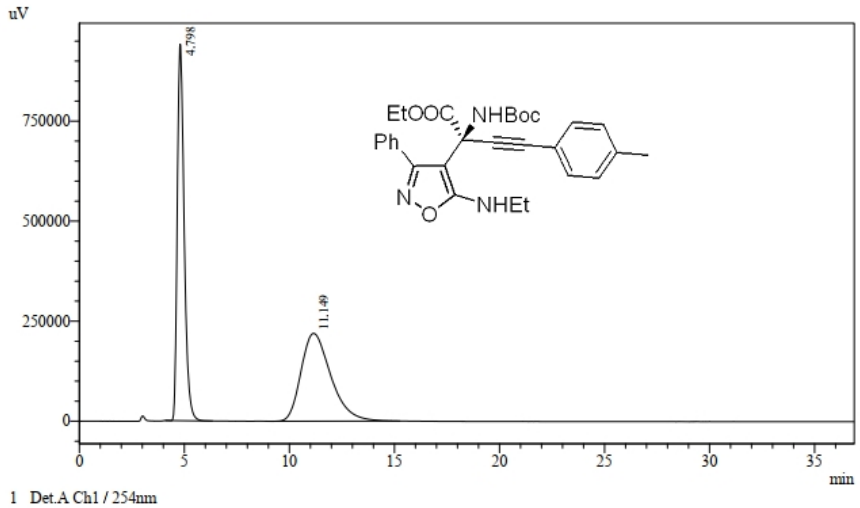


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.399	36651894	1603009	92.058	88.811
2	7.249	3161945	201956	7.942	11.189
Total		39813839	1804965	100.000	100.000

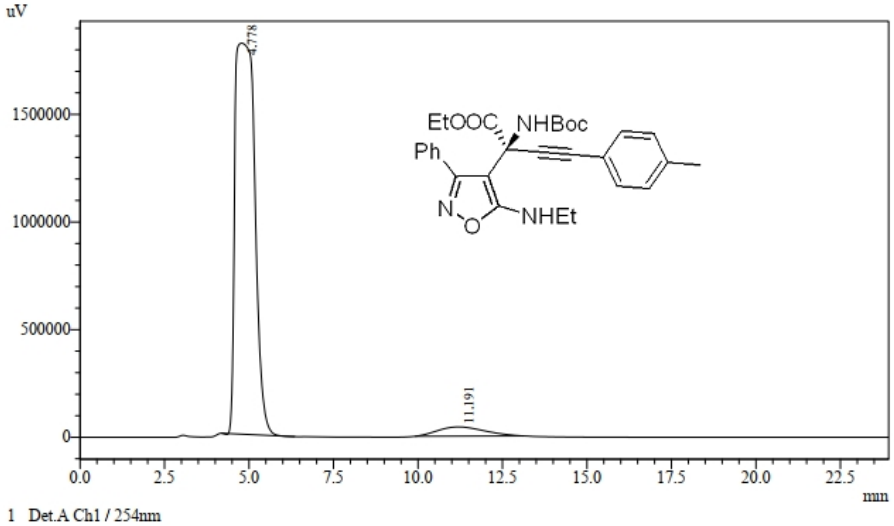
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(p-tolyl)but-3-ynoate (3ad)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.798	21419110	940712	49.720	81.086
2	11.149	21660163	219434	50.280	18.914
Total		43079273	1160146	100.000	100.000

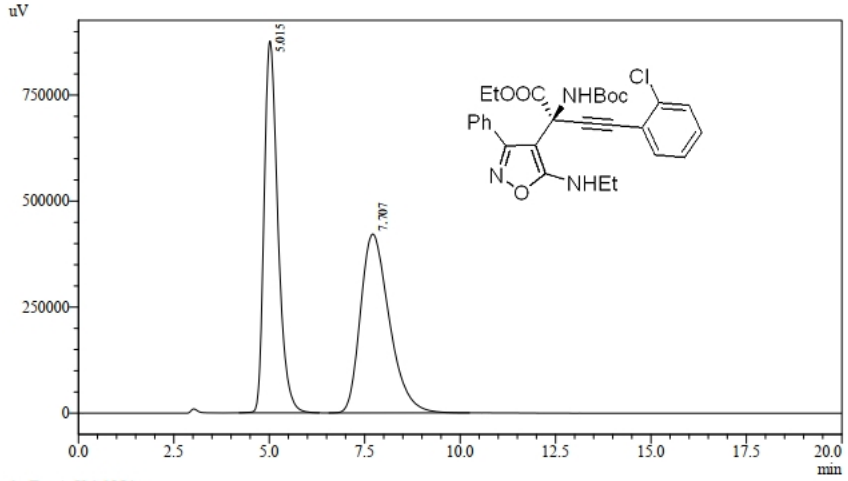


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.778	74144566	1816487	94.737	97.701
2	11.191	4118682	42744	5.263	2.299
Total		78263248	1859231	100.000	100.000

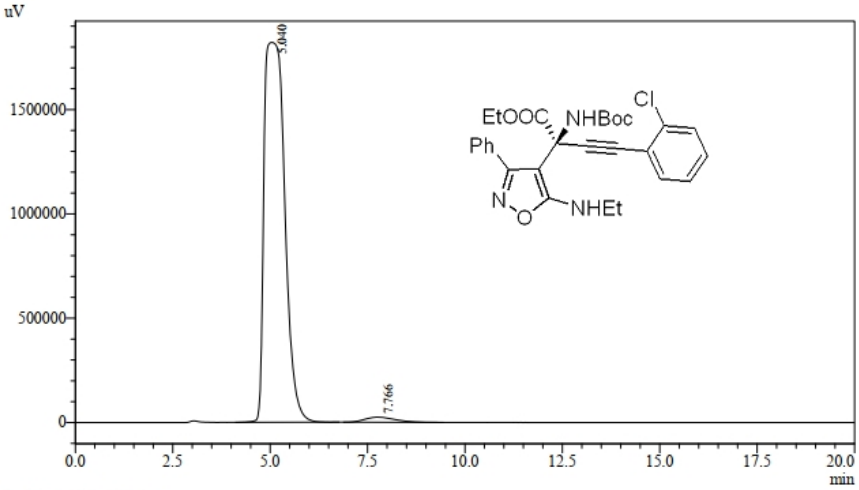
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(2-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ae)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.015	21992633	876636	49.759	67.520
2	7.707	22205834	421707	50.241	32.480
Total		44198467	1298343	100.000	100.000

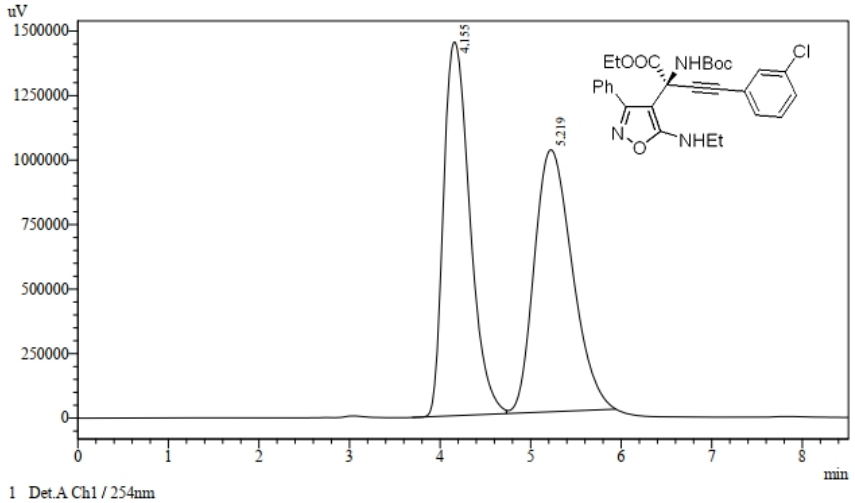


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.040	67112027	1821244	98.044	98.667
2	7.766	1339101	24601	1.956	1.333
Total		68451128	1845845	100.000	100.000

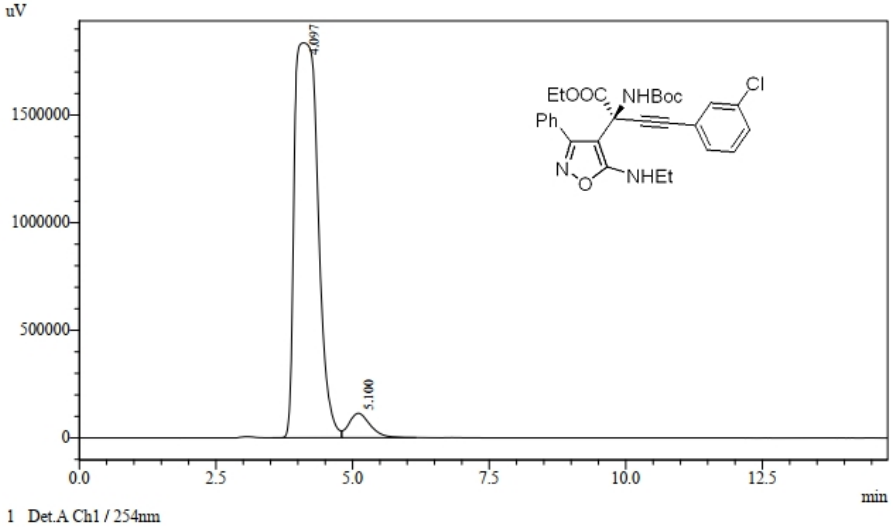
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(3-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3af)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.155	29317843	1448940	49.722	58.788
2	5.219	29645727	1015737	50.278	41.212
Total		58963570	2464677	100.000	100.000

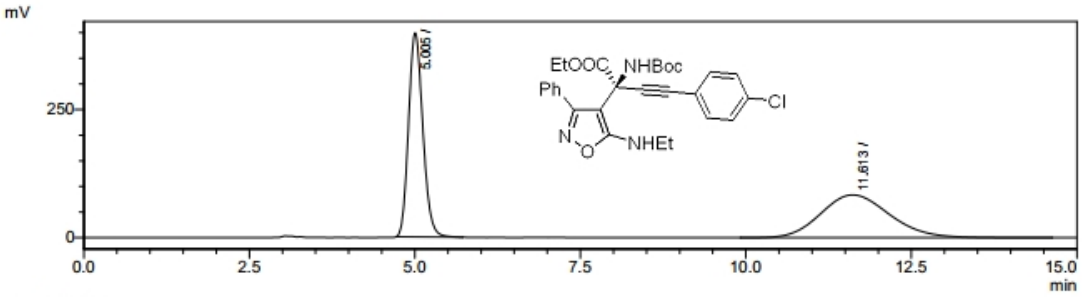


1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

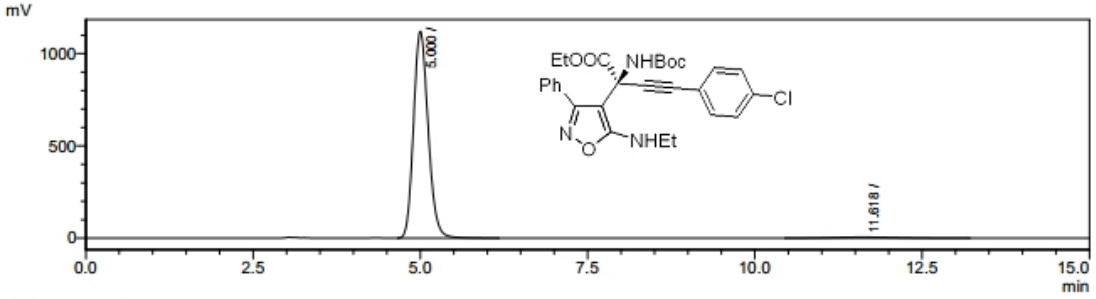
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.097	55099968	1834792	94.683	94.157
2	5.100	3094467	113868	5.317	5.843
Total		58194435	1948659	100.000	100.000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-(4-chlorophenyl)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ag)



检测器A 254nm

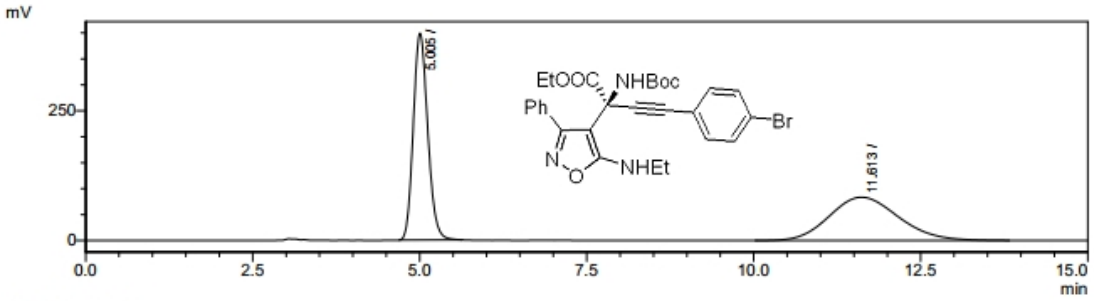
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.005	5979624	49.728	398112	82.671	49.728		M		
2	11.613	6045156	50.272	83451	17.329	50.272				
总计		12024780	100.000	481563	100.000					



检测器A 254nm

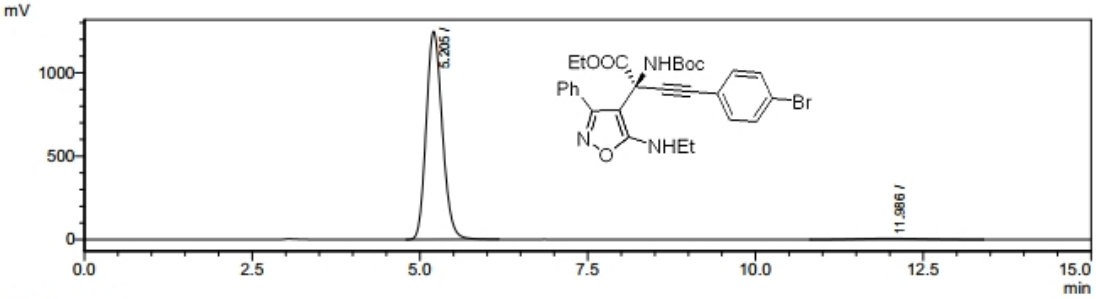
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.000	17039664	97.812	1121238	99.516	97.812		M		
2	11.618	381203	2.188	5457	0.484	2.188		M		
总计		17420867	100.000	1126695	100.000					

Ethyl (*S*)-4-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3ah)



检测器A 254nm

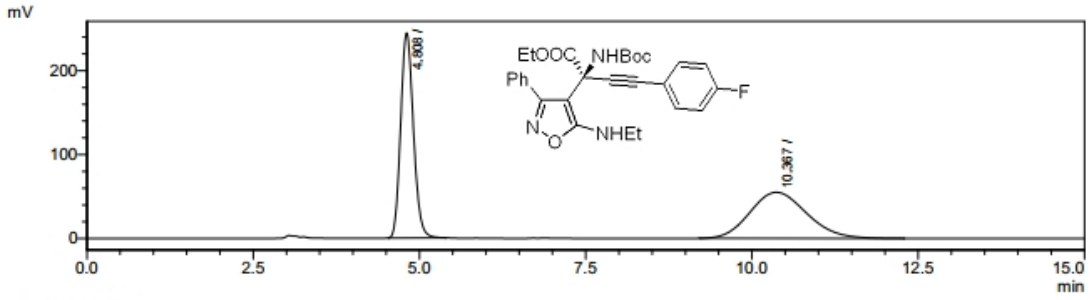
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.005	5989072	49.907	398486	82.704	49.907		M		
2	11.613	6011475	50.093	83335	17.296	50.093		M		
总计		12000547	100.000	481821	100.000					



检测器A 254nm

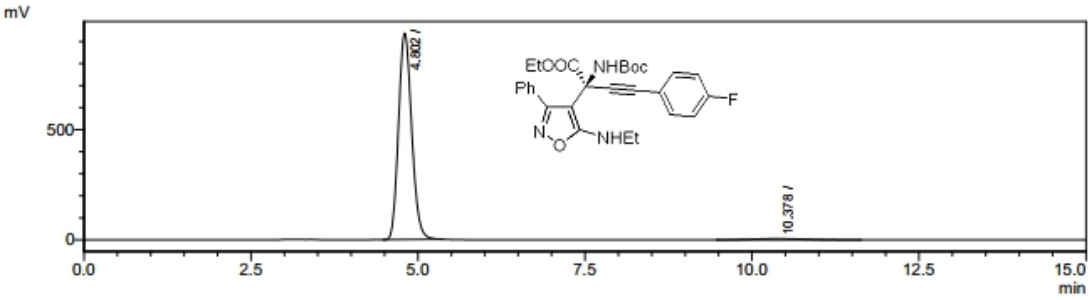
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	5.205	20844272	97.942	1247683	99.503	97.942		M		
2	11.986	438032	2.058	6231	0.497	2.058		M		
总计		21282304	100.000	1253913	100.000					

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(4-fluorophenyl)but-3-ynoate (3ai)



检测器A 254nm

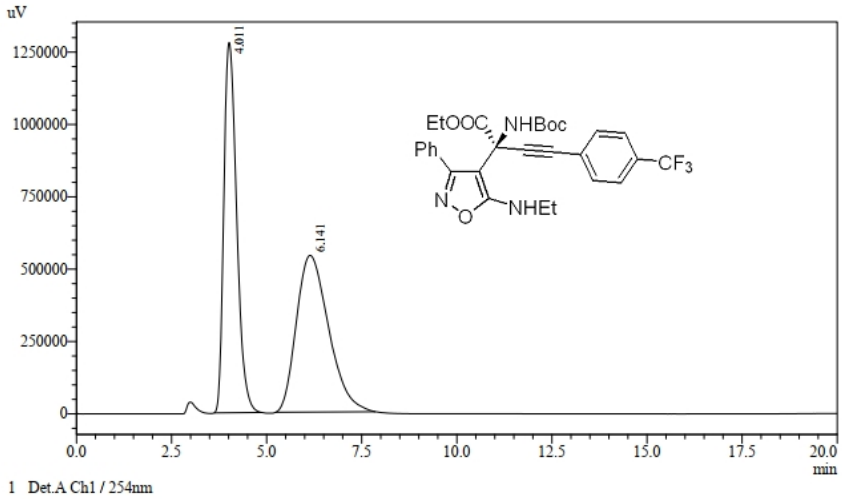
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	4.808	3253827	49.934	244517	81.658	49.934		M		
2	10.367	3262463	50.066	54922	18.342	50.066		M		
总计		6516290	100.000	299439	100.000					



检测器A 254nm

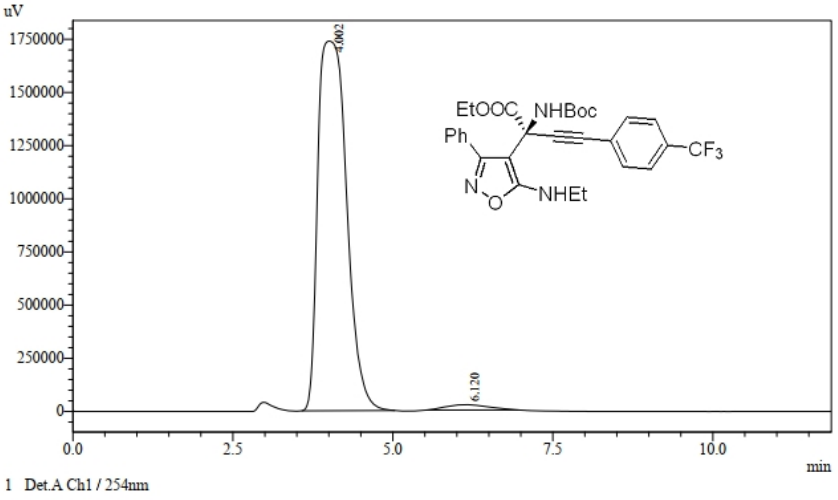
Peak#	Ret. Time	Area	Area%	Height	Height%	Conc.	Unit	Mark	ID#	Name
1	4.802	12847779	97.674	936876	99.429	97.674		M		
2	10.378	305931	2.326	5385	0.571	2.326		M		
总计		13153710	100.000	942261	100.000					

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(4-(trifluoromethyl)phenyl)but-3-ynoate (3aj)



Detector A Ch1 254nm

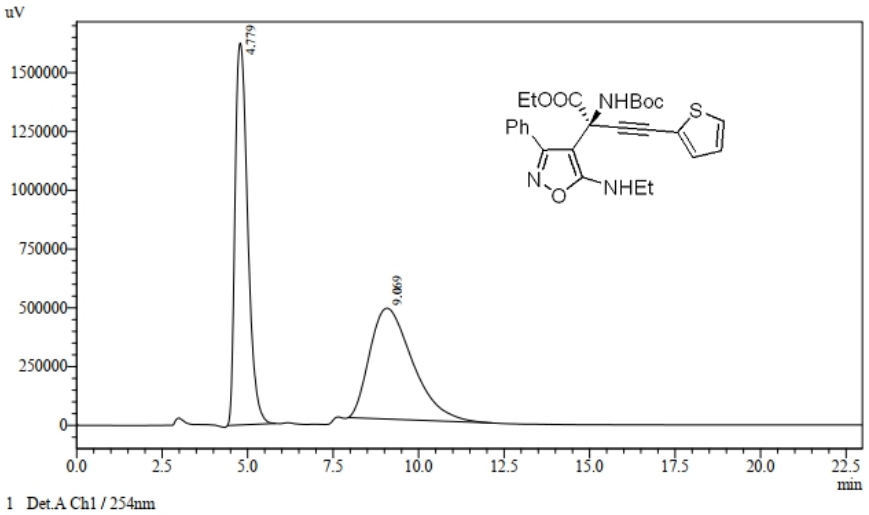
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.011	30043198	1278922	48.454	70.258
2	6.141	31960796	541411	51.546	29.742
Total		62003994	1820333	100.000	100.000



Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.002	54430182	1737687	97.878	98.580
2	6.120	1180115	25033	2.122	1.420
Total		55610297	1762721	100.000	100.000

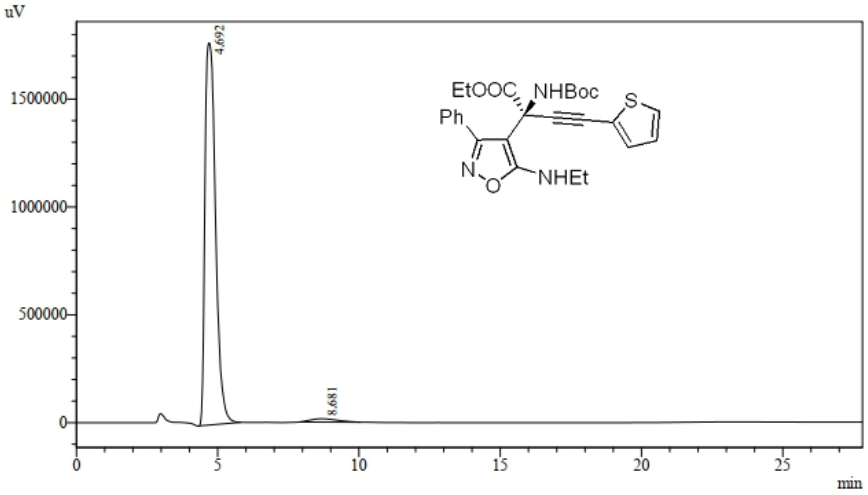
Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(thiophen-2-yl)but-3-ynoate (3ak)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.779	41648359	1623925	50.231	77.499
2	9.069	41266042	471501	49.769	22.501
Total		82914401	2095426	100.000	100.000

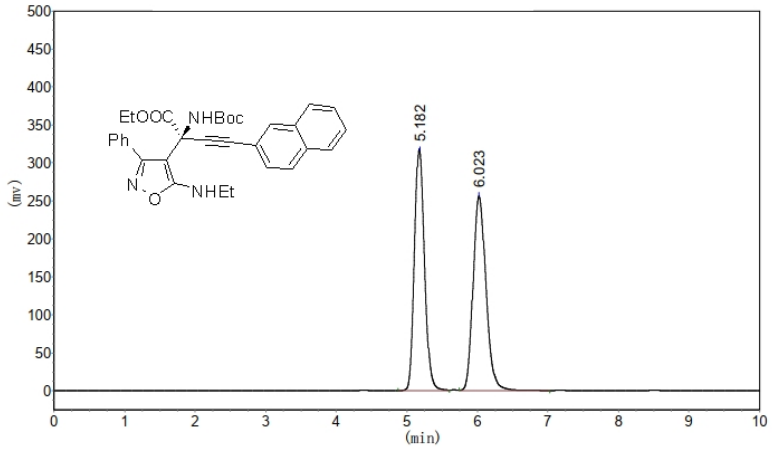


1 Det.A Ch1 / 254nm

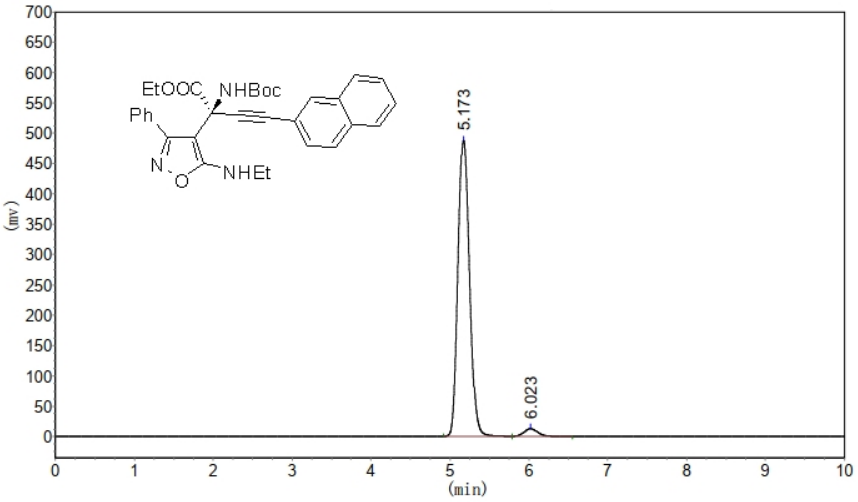
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.692	46147799	1771657	97.821	99.136
2	8.681	1028183	15446	2.179	0.864
Total		47175982	1787103	100.000	100.000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(naphthalen-2-yl)but-3-ynoate (3al)

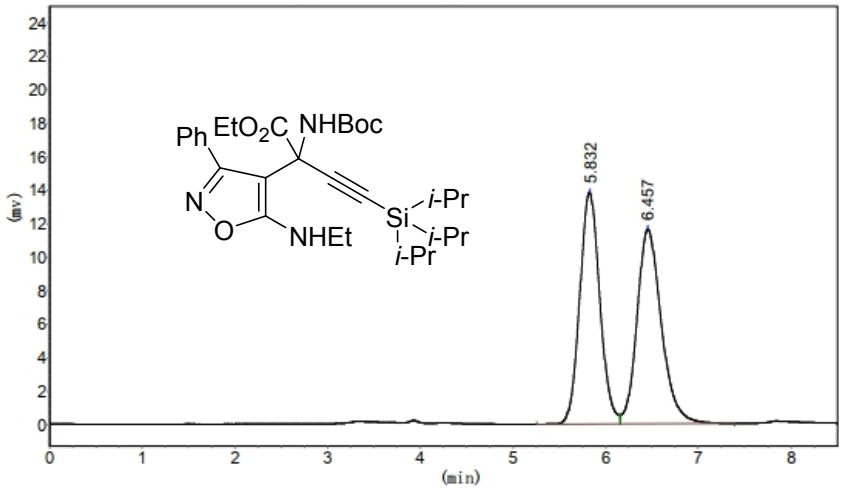


Peak#	Ret. Time	Hight	Area	Area%
1	5.182	317120.656	3179666.500	49.2000
2	6.023	255598.406	3283076.500	50.8000
Total		572719.063	6462743.000	100.0000

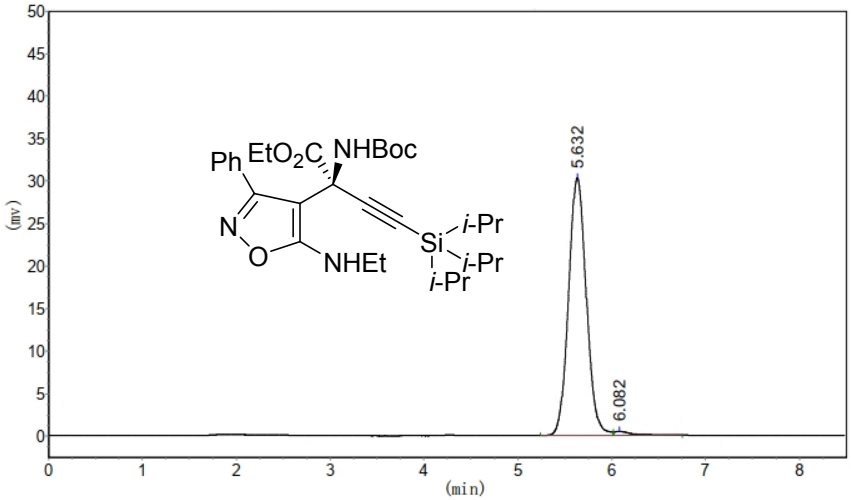


Peak#	Ret. Time	Hight	Area	Area%
1	5.173	487572.938	4992920.500	96.8632
2	6.023	13350.062	161689.188	3.1368
Total		500922.999	5154609.688	100.0000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-(triisopropylsilyl)but-3-ynoate (3am)

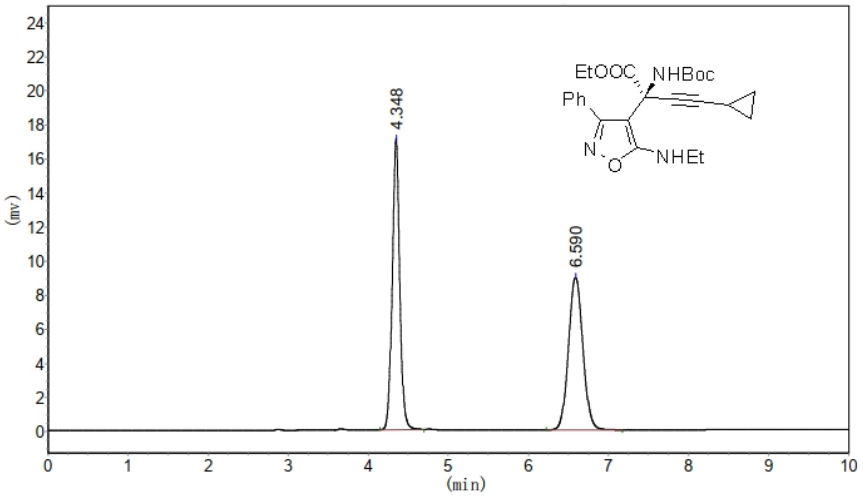


Peak#	Ret. Time	Hight	Area	Area%
1	5.832	13824.941	209000.922	49.5558
2	6.457	11613.313	212747.969	50.4442
Total		25438.254	421748.891	100.0000

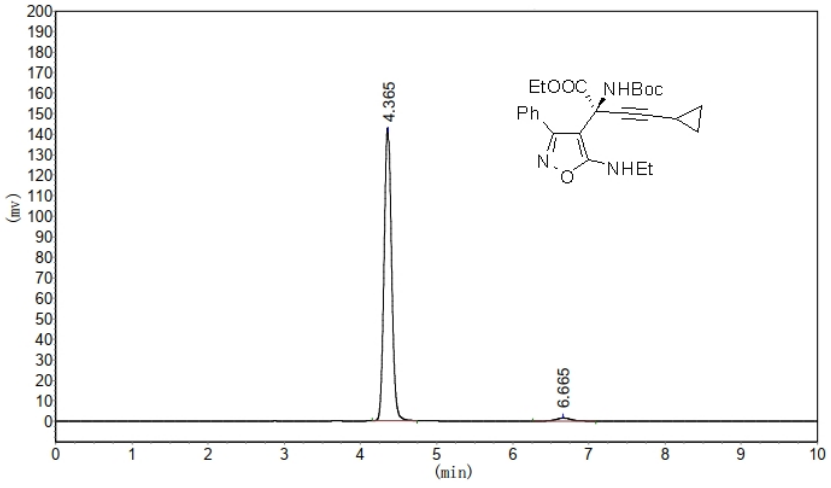


Peak#	Ret. Time	Hight	Area	Area%
1	5.632	30307.398	399915.000	98.3734
2	6.082	470.828	6612.474	1.6266
Total		30778.226	406527.474	100.0000

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-4-cyclopropyl-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)but-3-ynoate (3an)

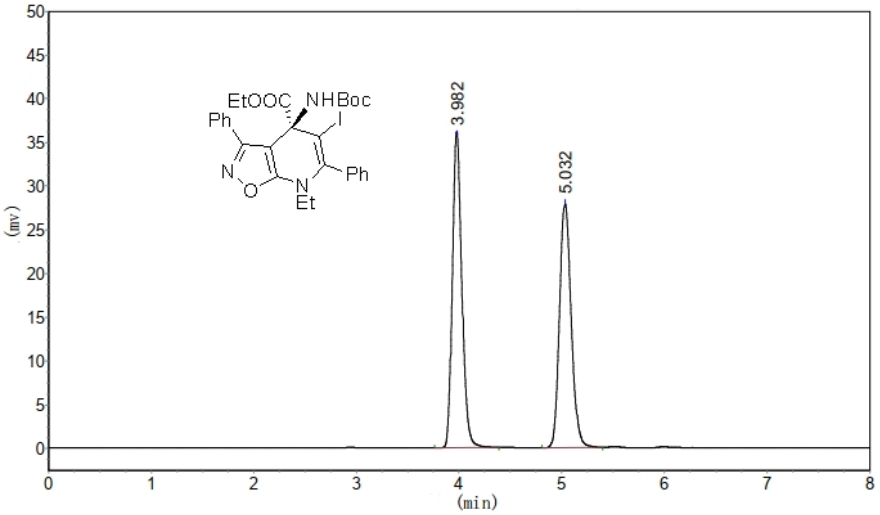


Peak#	Ret. Time	Hight	Area	Area%
1	4.348	17045.672	112062.148	50.0622
2	6.590	8924.982	111783.898	49.9378
Total		25970.654	223846.047	100.0000

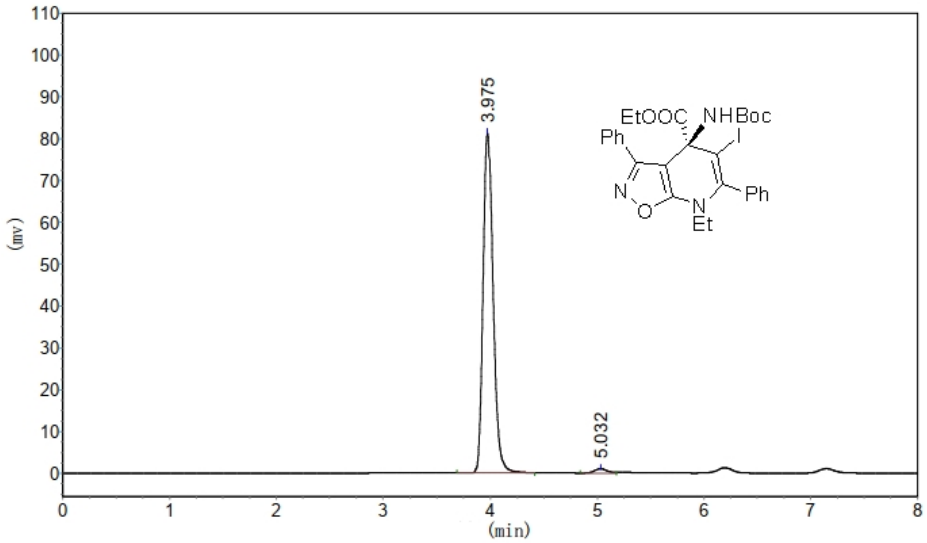


Peak#	Ret. Time	Hight	Area	Area%
1	4.365	141911.578	965790.313	98.0019
2	6.665	1529.550	19690.801	1.9981
Total		143441.128	985481.113	100.0000

Ethyl (*S*)-4-((*tert*-butoxycarbonyl)amino)-7-ethyl-5-iodo-3,6-diphenyl-4,7-dihydroisoxazolo[5,4-b]pyridine-4-carboxylate (4)

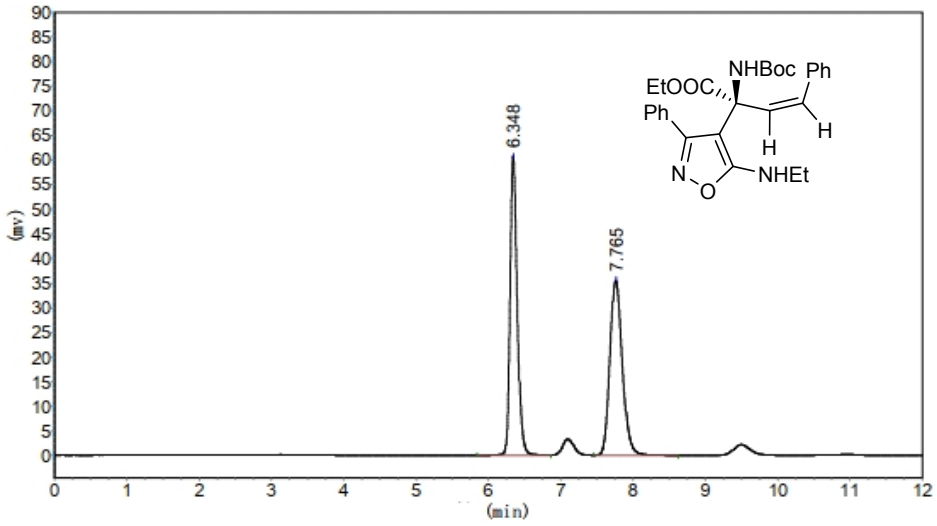


Peak#	Ret. Time	Hight	Area	Area%
1	3.982	36011.637	233801.656	51.3425
2	5.032	27812.297	221575.031	48.6575
Total		63823.934	455376.688	100.0000

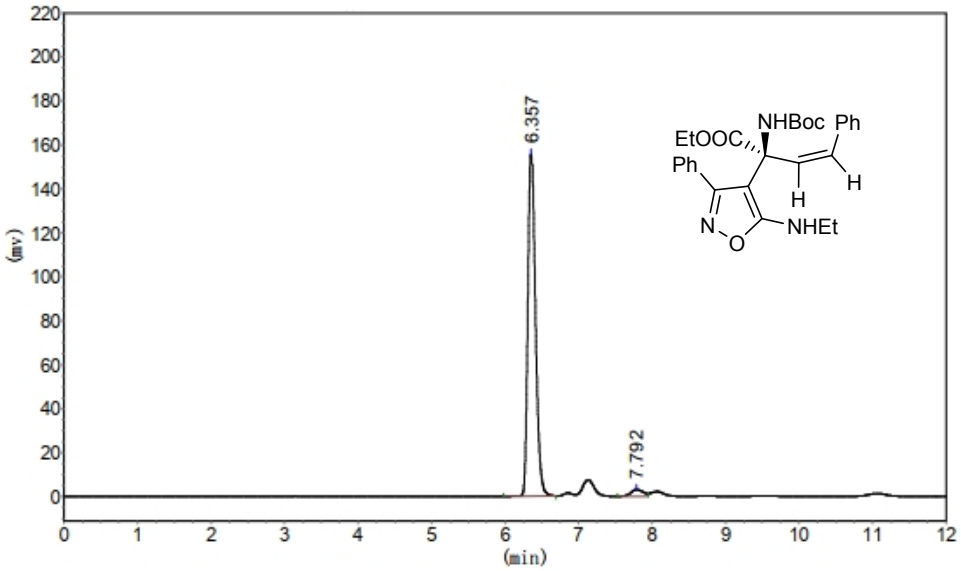


Peak#	Ret. Time	Hight	Area	Area%
1	3.975	81170.508	530482.313	98.3773
2	5.032	1082.000	8750.200	1.6227
Total		82252.508	539232.513	100.0000

Ethyl (*S*,*Z*)-2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol -4-yl)-4-phenylbut-3-enoate (5)

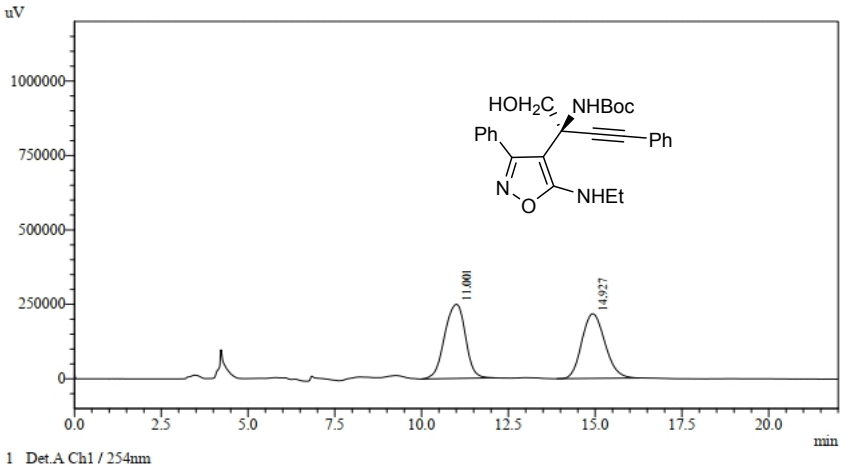


Peak#	Ret.Time	Hight	Area	Area%
1	6.348	60597.199	426247.563	50.0539
2	7.765	35450.094	425328.844	49.9461
Total		96047.293	851576.406	100.0000



Peak#	Ret.Time	Hight	Area	Area%
1	6.357	155609.328	1100915.875	96.6391
2	7.792	3243.000	38287.699	3.3609
Total		158852.328	1139203.574	100.0000

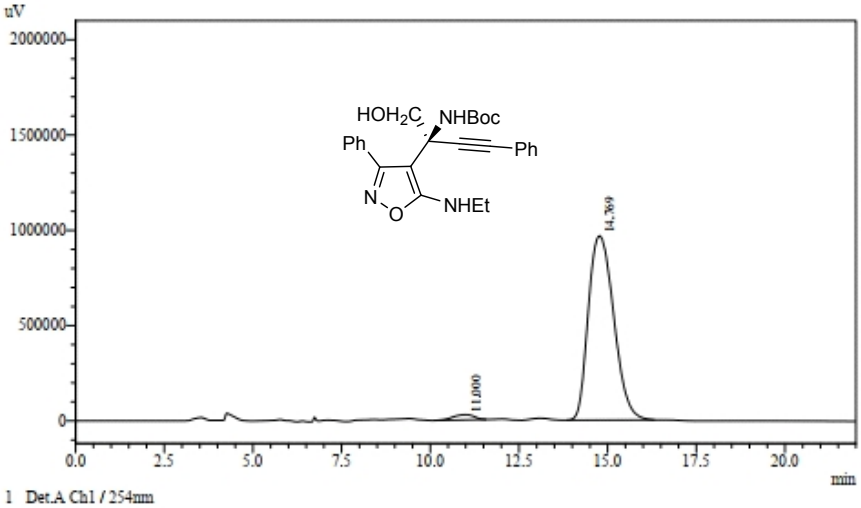
tert-butyl (_S_)-(2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-1-hydroxy-4-phenylbut-3-yn-2-yl)carbamate (6)



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.001	10416697	249215	50.822	53.447
2	14.927	10079909	217070	49.178	46.553
Total		20496605	466285	100.000	100.000

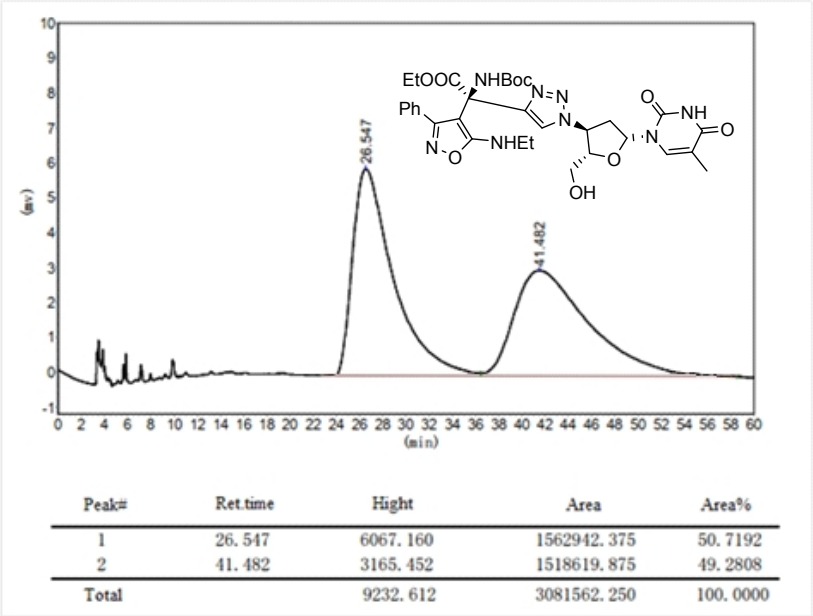


1 Det.A Ch1 / 254nm

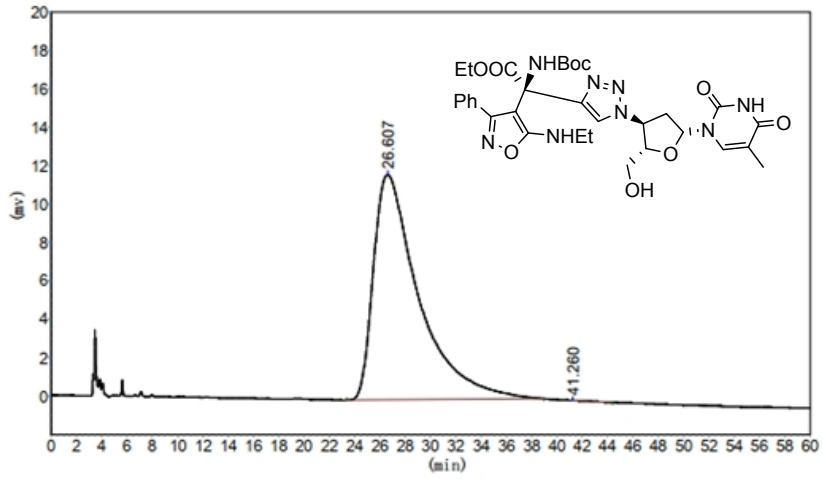
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.000	1124810	27052	2.275	2.724
2	14.769	48309331	966176	97.725	97.276
Total		49434140	993228	100.000	100.000

Ethyl 2-((*tert*-butoxycarbonyl)amino)-2-(5-(ethylamino)-3-phenylisoxazol-4-yl)-2-(1-((2*S*,3*S*,5*R*)-2-(hydroxymethyl)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3-yl)-1H-1,2,3-triazol-4-yl)acetate (8)



Peak#	Ret.time	Hight	Area	Area%
1	26.547	6067.160	1562942.375	50.7192
2	41.482	3165.452	1518619.875	49.2808
Total		9232.612	3081562.250	100.0000



Peak#	Ret.Time	Hight	Area	Area%
1	26.607	11720.568	2915100.500	99.9785
2	41.260	2.296	626.100	0.0215
Total		11722.865	2915726.600	100.0000